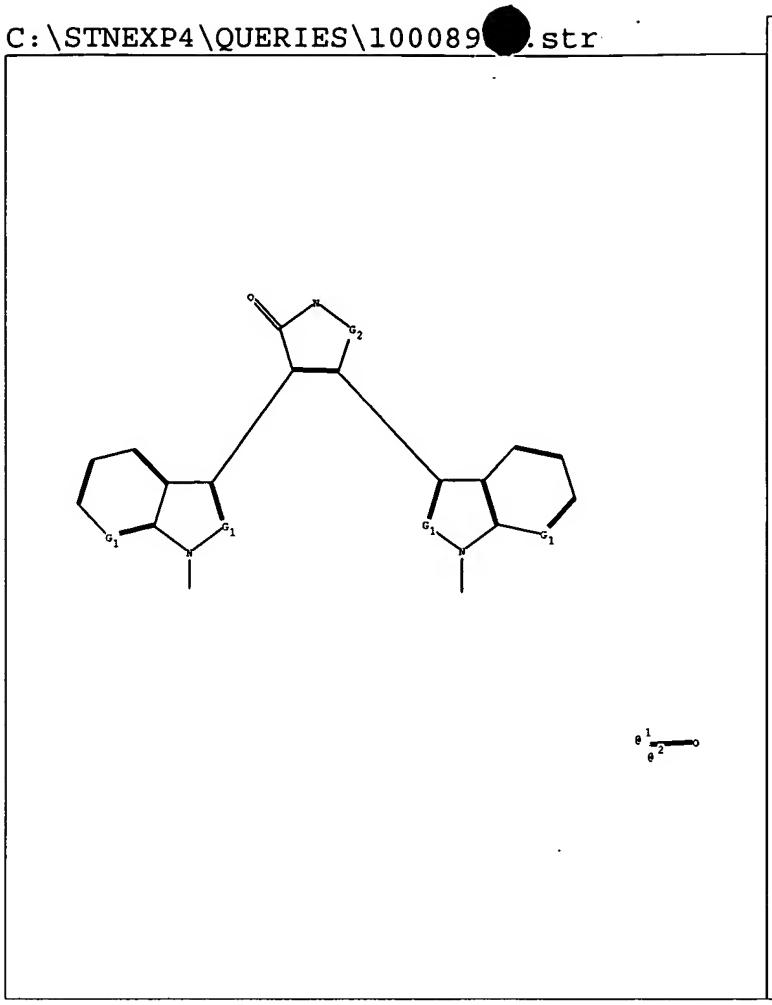
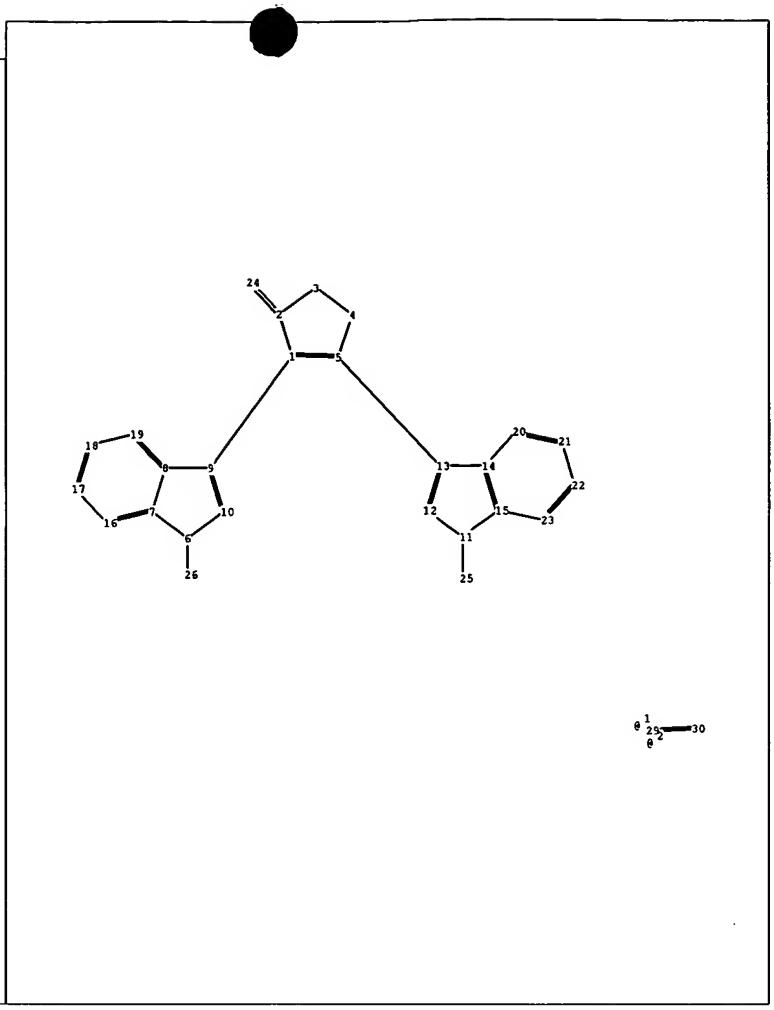
C:\STNEXP4\QUERIES\100089[redacted].str





chain nodes :
24 29 30
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
22 23 25 26
chain bonds :
2-24 29-30
ring bonds :
1-2 1-5 1-9 2-3 3-4 4-5 5-13 6-7 6-10 6-26 7-8 7-16 8-9 8-19
9-10 11-12 11-15 11-25 12-13 13-14 14-15 14-20 15-23 16-17
17-18 18-19 20-21 21-22 22-23
exact/norm bonds :
1-2 1-5 1-9 2-3 2-24 3-4 4-5 5-13 6-7 6-10 6-26 7-8 7-16 8-9
8-19 9-10 11-12 11-15 11-25 12-13 13-14 14-15 14-20 15-23 16-17
17-18 18-19 20-21 21-22 22-23 29-30

G1:C,N

G2:CH,[*1-*2]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom
10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom
18:Atom 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:CLASS 25:Atom
26:Atom 29:CLASS 30:CLASS

```
=> d his

     (FILE 'HOME' ENTERED AT 18:34:50 ON 15 SEP 2003)

     FILE 'REGISTRY' ENTERED AT 18:34:57 ON 15 SEP 2003
L1             STRUCTURE UPLOADED
L2             QUE L1
L3           50 S L2
L4         2334 S L2 SSS FUL
L5             STRUCTURE UPLOADED
L6             QUE L5
L7           50 S L6
L8         2293 S L6  SUB=L4 FUL

     FILE 'CAPLUS' ENTERED AT 18:44:04 ON 15 SEP 2003
L9         2013 S L8
L10         ANALYZE L9 1- RN HIT :    2281 TERMS

     FILE 'REGISTRY' ENTERED AT 18:45:26 ON 15 SEP 2003
L11           1 S 62996-74-1/RN
L12           1 S 99533-80-9/RN
L13           1 S 112953-11-4/RN
L14           1 S 120685-11-2/RN
L15           1 S 108068-98-0/RN
L16           1 S 99570-78-2/RN
L17         100 S 169939?/RN
L18         100 S 156177?/RN
L19         100 S 126643?/RN
L20          15 S L8 AND L17
L21          36 S L8 AND L18
L22           2 S L8 AND L19
L23        2249 S L8 NOT (L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR L21 OR L22)

     FILE 'CAPLUS' ENTERED AT 18:48:42 ON 15 SEP 2003
L24         323 S L23
L25         ANALYZE L24 1- RN HIT :    2237 TERMS

     FILE 'REGISTRY' ENTERED AT 18:49:33 ON 15 SEP 2003
L26           1 S 169939-94-0/RN
L27         100 S 111358?/RN
L28           1 S 169939-93-9/RN
L29         100 S 118735?/RN
L30          15 S L23 AND L27
L31          34 S L23 AND L29
L32        2201 S L23 NOT (L30 OR L31)

     FILE 'CAPLUS' ENTERED AT 18:56:56 ON 15 SEP 2003
L33         314 S L32

     FILE 'REGISTRY' ENTERED AT 18:57:48 ON 15 SEP 2003
L34        1036 S 32739.1/RID — excluded
L35         942 S L32 AND L34
L36        1259 S L32 NOT L35

     FILE 'CAPLUS' ENTERED AT 18:58:54 ON 15 SEP 2003

     FILE 'REGISTRY' ENTERED AT 18:59:13 ON 15 SEP 2003
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FILE 'CAPLUS' ENTERED AT 18:59:13 ON 15 SEP 2003

FILE 'REGISTRY' ENTERED AT 18:59:17 ON 15 SEP 2003
L37 866 S 22650.1/RID — excluded
L38 818 S L36 AND L37
L39 441 S L36 NOT L38

FILE 'CAPLUS' ENTERED AT 19:00:12 ON 15 SEP 2003
L40 114 S L39

FILE 'REGISTRY' ENTERED AT 19:00:31 ON 15 SEP 2003

FILE 'CAPLUS' ENTERED AT 19:00:32 ON 15 SEP 2003

FILE 'REGISTRY' ENTERED AT 19:00:38 ON 15 SEP 2003

FILE 'CAPLUS' ENTERED AT 19:00:38 ON 15 SEP 2003

FILE 'REGISTRY' ENTERED AT 19:00:43 ON 15 SEP 2003

FILE 'CAPLUS' ENTERED AT 19:00:44 ON 15 SEP 2003

FILE 'REGISTRY' ENTERED AT 19:00:51 ON 15 SEP 2003

FILE 'CAPLUS' ENTERED AT 19:00:52 ON 15 SEP 2003

FILE 'REGISTRY' ENTERED AT 19:00:55 ON 15 SEP 2003
L41 1023 S L8 AND L34
L42 825 S L8 AND L37
L43 1848 S L41 OR L42
L44 445 S L8 NOT L43
L45 4 S L44 NOT L39
L46 17 S 39828.3/RID excluded
L47 15 S L44 AND L46
L48 430 S L44 NOT L47

FILE 'CAPLUS' ENTERED AT 19:03:41 ON 15 SEP 2003
L49 114 S L48

FILE 'REGISTRY' ENTERED AT 19:04:34 ON 15 SEP 2003
L50 89 S 63638.1/RID — excluded
L51 87 S L48 AND L50
L52 343 S L48 NOT L51

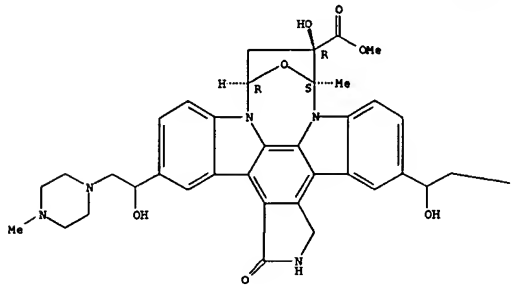
FILE 'CAPLUS' ENTERED AT 19:06:54 ON 15 SEP 2003
L53 53 S L52 Printed
L54 67 S L51 transcript ran in error 10008982
L55 6 S L53 AND L54

=> d scan l34
YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y)/N:y

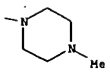
L34 1036 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN 9,12-Epoxy-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10-carboxylic acid, 2,3,9,10,11,12-hexahydro-10-hydroxy-5,16-bis[1-hydroxy-2-(4-methyl-1-piperazinyl)ethyl]-9-methyl-1-oxo-, methyl ester, (9S,10R,12R)- (9CI)
MF C41 H49 N7 O7

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



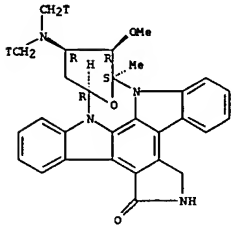
L34 1036 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN (Continued)

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

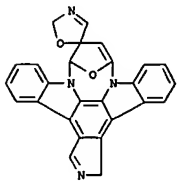
L37 866 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN 9,13-Epoxy-1H,9H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonin-1-one, 11-[di(methyl-t)amino]-2,3,10,11,12,13-hexahydro-10-methoxy-9-methyl-, (9S,10R,11R,13R)- (9CI)
MF C29 HZ6 N4 O3 T2

Absolute stereochemistry.



HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

L46 17 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN Spiro[9,12-epoxy-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10(9H),5'(2'H)-oxazole] (9CI)
MF C26 H16 N4 O2
CI RPS

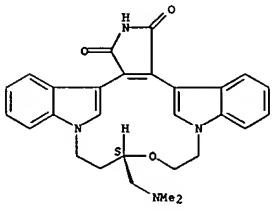


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

L51 87 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN 9H,16H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-16,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, (9S)-(9CI)
MF C28 H28 N4 O3 . Cl H

Absolute stereochemistry.



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good use later

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

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=> d his

     (FILE 'HOME' ENTERED AT 18:34:50 ON 15 SEP 2003)

     FILE 'REGISTRY' ENTERED AT 18:34:57 ON 15 SEP 2003
L1             STRUCTURE UPLOADED
L2             QUE L1
L3           50 S L2
L4         2334 S L2 SSS FUL
L5             STRUCTURE UPLOADED
L6             QUE L5
L7           50 S L6
L8         2293 S L6  SUB=L4 FUL

     FILE 'CAPLUS' ENTERED AT 18:44:04 ON 15 SEP 2003
L9         2013 S L8
L10         ANALYZE L9 1- RN HIT :    2281 TERMS

     FILE 'REGISTRY' ENTERED AT 18:45:26 ON 15 SEP 2003
L11           1 S 62996-74-1/RN
L12           1 S 99533-80-9/RN
L13           1 S 112953-11-4/RN
L14           1 S 120685-11-2/RN
L15           1 S 108068-98-0/RN
L16           1 S 99570-78-2/RN
L17         100 S 169939?/RN
L18         100 S 156177?/RN
L19         100 S 126643?/RN
L20          15 S L8 AND L17
L21          36 S L8 AND L18
L22           2 S L8 AND L19
L23        2249 S L8 NOT (L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR L21 OR L22)

     FILE 'CAPLUS' ENTERED AT 18:48:42 ON 15 SEP 2003
L24         323 S L23
L25         ANALYZE L24 1- RN HIT :    2237 TERMS

     FILE 'REGISTRY' ENTERED AT 18:49:33 ON 15 SEP 2003
L26           1 S 169939-94-0/RN
L27         100 S 111358?/RN
L28           1 S 169939-93-9/RN
L29         100 S 118735?/RN
L30          15 S L23 AND L27
L31          34 S L23 AND L29
L32        2201 S L23 NOT (L30 OR L31)

     FILE 'CAPLUS' ENTERED AT 18:56:56 ON 15 SEP 2003
L33         314 S L32

     FILE 'REGISTRY' ENTERED AT 18:57:48 ON 15 SEP 2003
L34        1036 S 32739.1/RID
L35         942 S L32 AND L34
L36        1259 S L32 NOT L35

     FILE 'CAPLUS' ENTERED AT 18:58:54 ON 15 SEP 2003

     FILE 'REGISTRY' ENTERED AT 18:59:13 ON 15 SEP 2003
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     FILE 'CAPLUS' ENTERED AT 18:59:13 ON 15 SEP 2003

     FILE 'REGISTRY' ENTERED AT 18:59:17 ON 15 SEP 2003
L37          866 S 22650.1/RID
L38          818 S L36 AND L37
L39          441 S L36 NOT L38

     FILE 'CAPLUS' ENTERED AT 19:00:12 ON 15 SEP 2003
L40          114 S L39

     FILE 'REGISTRY' ENTERED AT 19:00:31 ON 15 SEP 2003

     FILE 'CAPLUS' ENTERED AT 19:00:32 ON 15 SEP 2003

     FILE 'REGISTRY' ENTERED AT 19:00:38 ON 15 SEP 2003

     FILE 'CAPLUS' ENTERED AT 19:00:38 ON 15 SEP 2003

     FILE 'REGISTRY' ENTERED AT 19:00:43 ON 15 SEP 2003

     FILE 'CAPLUS' ENTERED AT 19:00:44 ON 15 SEP 2003

     FILE 'REGISTRY' ENTERED AT 19:00:51 ON 15 SEP 2003

     FILE 'CAPLUS' ENTERED AT 19:00:52 ON 15 SEP 2003

     FILE 'REGISTRY' ENTERED AT 19:00:55 ON 15 SEP 2003
L41         1023 S L8 AND L34
L42          825 S L8 AND L37
L43         1848 S L41 OR L42
L44          445 S L8 NOT L43
L45            4 S L44 NOT L39
L46           17 S 39828.3/RID
L47           15 S L44 AND L46
L48          430 S L44 NOT L47

     FILE 'CAPLUS' ENTERED AT 19:03:41 ON 15 SEP 2003
L49          114 S L48

     FILE 'REGISTRY' ENTERED AT 19:04:34 ON 15 SEP 2003
L50           89 S 63638.1/RID
L51           87 S L48 AND L50
L52          343 S L48 NOT L51

     FILE 'CAPLUS' ENTERED AT 19:06:54 ON 15 SEP 2003
L53           53 S L52
L54           67 S L51
L55            6 S L53 AND L54

     FILE 'REGISTRY' ENTERED AT 19:12:00 ON 15 SEP 2003

     FILE 'CAPLUS' ENTERED AT 19:12:11 ON 15 SEP 2003

     FILE 'REGISTRY' ENTERED AT 19:12:17 ON 15 SEP 2003

     FILE 'CAPLUS' ENTERED AT 19:12:42 ON 15 SEP 2003

     FILE 'REGISTRY' ENTERED AT 19:12:47 ON 15 SEP 2003
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FILE 'CAPLUS' ENTERED AT 19:13:06 ON 15 SEP 2003

FILE 'REGISTRY' ENTERED AT 19:13:10 ON 15 SEP 2003

FILE 'CAPLUS' ENTERED AT 19:13:22 ON 15 SEP 2003

=> d ibib abs hitstr l53 1-53

L53 ANSWER 1 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:109026 CAPLUS
DOCUMENT NUMBER: 139:46604
TITLE: DNA targeting of two new antitumour rebeccamycin derivatives
AUTHOR(S): Facompre, Michael; Baldeyrou, Brigitte; Bailly, Christian; Anizon, Fabrice; Marminon, Christelle; Prudhomme, Michelle; Colson, Pierre; Houssier, Claude
CORPORATE SOURCE: Laboratoire de Pharmacologie Antitumorale du Centre Oscar Lambret, IRCL, INSERM U524 et Laboratoire de Pharmacologie Antitumorale du Centre Oscar Lambret, IRCL, Lille, 59045, Fr.
SOURCE: European Journal of Medicinal Chemistry (2002), 37(12), 925-932
CODEN: EJMCA5; ISSN: 0223-5234
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

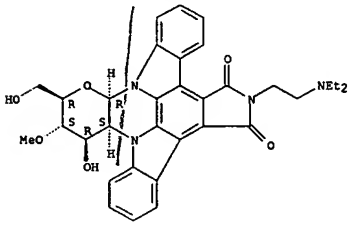
AB In the course of a medicinal chem. program aimed at discovering novel tumor-active rebeccamycin derivs. targeting DNA and/or topoisomerase I, a series of analogs with the sugar residue linked to the two indole nitrogens was recently developed. Two promising drug candidates in this staurosporine-rebeccamycin hybrid series were selected for a DNA-binding study reported here. The DNA interaction of the cationic indolocarbazole glycosides MP059 bearing a N,N-diethylaminoethyl side chain and MP072 contg. a sugar bearing an amino group was compared with that of the uncharged analog MP024. The results show that the addn. of a cationic substituent, either directly on the indolocarbazole chromophore or on the carbohydrate residue, significantly reinforces the interaction of the drugs with nucleic acids. The two cationic mols. MP059 and MP072 recognize preferentially sequences contg. GpT.cntdot.ApC and TpG.cntdot.CpA steps but they do not inhibit topoisomerase I, in contrast to the parent uncharged deriv. MP024 which stimulates DNA single strand breaks by topoisomerase I. The cytotoxic activity of the indolocarbazole derivs. bearing pos. charged groups is one order of magnitude higher than that of the neutral compd. MP024. The high cytotoxic potential can be attributed to the enhanced DNA binding and sequence recognition capacity of the cationic compds. The study provides useful information for further structure-activity relationship studies in the indolocarbazole series.

IT 340162-41-6, MP 024 340162-60-9, MP 072
546114-92-5, MP 059
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DNA targeting of two new antitumor rebeccamycin derivs.)

RN 340162-41-6 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 5a,8,9,9a-tetrahydro-9,16-dihydroxy-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L53 ANSWER 1 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
Absolute stereochemistry.



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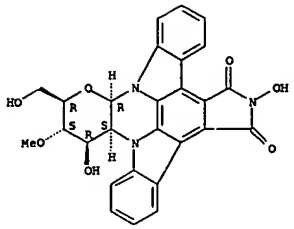
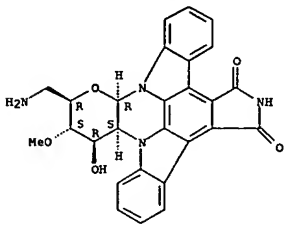
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 1 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 340162-60-9 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 7-(aminomethyl)-5a,8,9,9a-tetrahydro-9-hydroxy-8-methoxy-, monohydrochloride, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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RN 546114-92-5 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 16-[2-(diethylamino)ethyl]-5a,8,9,9a-tetrahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-, monohydrochloride, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

applicant

L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:449687 CAPLUS
DOCUMENT NUMBER: 137:33328
TITLE: Preparation of bis(heterocyclyl)pyrrolinones and bis(heterocyclyl)pyrrolediones as inhibitors of kinases for the treatment of kinase-mediated diseases
INVENTOR(S): Kuo, Gee-Hong; Prouty, Catherine; Deangelis, Alan; Zhang, Han-Cheng
PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 143 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

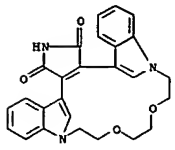
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002046197	A1	20020613	WO 2001-US47866	20011206
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002027371	A5	20020618	AU 2002-27371	20011206
US 2003078280	A1	20030424	US 2001-8982	20011206
PRIORITY APPLN. INFO.:			US 2000-254161P P	20001208
			WO 2001-US47866 W	20011206
OTHER SOURCE(S):		MARPAT 137:33328		

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

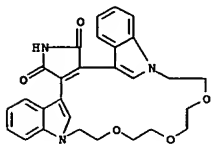
AB Bis(heterocyclyl)pyrrolinones or bis(heterocyclyl)pyrrolediones I (A, A1, E, E1 = HC, N; Z = O, H2; R1, R3 = H, OH, NO2, halo, cyano, (un)substituted alkyl, alkenyl, alkynyl, amino; R2 = alkanediyl, alkenediyl, alkynediyl, oxyalkyloxy, oxyalkenyloxy, etc.; R4, R5 = alkyl, alkenyl, alkynyl, oxoalkyl, oxoalkenyl, oxoalkynyl) linking the heterocyclyl moieties into macrocycles are prepd. as inhibitors for kinases such as protein kinase C and glycogen synthase kinase 3.beta. in the treatment of kinase-mediated and dual-kinase mediated diseases such as diabetes, cancer, cardiovascular diseases such as stroke, immunol. disorders such as transplant rejection, and dermatol. disorders such as psoriasis and baldness. E.g., stannylation of iodopyrrolopyridine II, coupling of the stannane with N-methyl-3,4-dichloromaleimide and loss of the Boc groups, macrocyclocondensation of the bis(pyrrolopyridyl)maleimide with tri(ethylene glycol) dimesylate and Cs2CO3 in DMF, hydrolysis of the maleimide to a maleic anhydride, and amidation of the anhydride with hexamethyldisilazide gave the macrocycle III. Biol. data on the inhibition of kinases and the selectivity of the kinase inhibition by compds. of the invention is given. E.g., III inhibits GSK-3.beta. at 0.027 .mu.M, and inhibits protein kinase C isoforms at 2-38 .mu.M while showing inhibition of other kinases such as VEGF-R and PKC-.alpha. at >10

L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
.mu.M (<50 % inhibition at the highest doses tested).
IT 436866-50-1P 436866-51-2P 436866-52-3P
436866-53-4P 436866-54-5P 436866-55-6P
436866-56-7P 436866-57-8P 436866-58-9P
436866-59-0P 436866-60-3P 436866-61-4P
436866-62-5P 436866-63-6P 436866-64-7P
436866-65-8P 436866-66-9P 436866-67-0P
436866-68-1P 436866-69-2P 436866-70-5P
436866-71-6P 436866-72-7P 436866-73-8P
436866-74-9P 436866-75-0P 436866-76-1P
436866-77-2P 436866-78-3P 436866-79-4P
436866-80-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compd.; prepn. of bis(heterocyclyl)pyrrolinones and bis(heterocyclyl)pyrrolediones as inhibitors of kinases for the treatment of kinase-mediated diseases such as diabetes, stroke, transplant rejection, psoriasis, and baldness)
RN 436866-50-1 CAPLUS
CN 5,23:14,19-Dimetheno-20H-dibenzo[h,n]pyrrolo[3,4-k][1,4,7,16]dioxadiazacyclooctadecine-20,22(21H)-dione, 6,7,9,10,12,13-hexahydro- (9CI) (CA INDEX NAME)

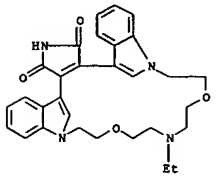


540-469
514-410

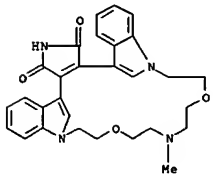
RN 436866-51-2 CAPLUS
CN 5,26:17,22-Dimetheno-23H-dibenzo[k,q]pyrrolo[3,4-n][1,4,7,10,19]trioxadiazacycloheneicosine-23,25(24H)-dione, 6,7,9,10,12,13,15,16-octahydro- (9CI) (CA INDEX NAME)



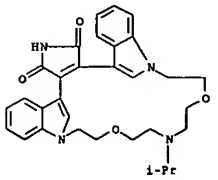
L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 436866-55-6 CAPLUS
CN 5,26:17,22-Dimetheno-9H,23H-dibenzo[k,q]pyrrolo[3,4-n][1,7,4,10,19]dioxatriazacycloheneicosine-23,25(24H)-dione, 6,7,10,11,12,13,15,16-octahydro-11-methyl- (9CI) (CA INDEX NAME)

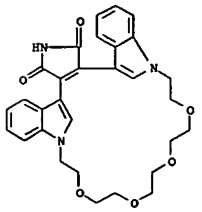


RN 436866-56-7 CAPLUS
CN 5,26:17,22-Dimetheno-9H,23H-dibenzo[k,q]pyrrolo[3,4-n][1,7,4,10,19]dioxatriazacycloheneicosine-23,25(24H)-dione, 6,7,10,11,12,13,15,16-octahydro-11-(1-methylethyl)- (9CI) (CA INDEX NAME)

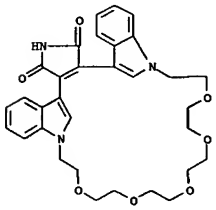


RN 436866-57-8 CAPLUS

L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
RN 436866-52-3 CAPLUS
CN 5,29:20,25-Dimetheno-26H-dibenzo[n,t]pyrrolo[3,4-q][1,4,7,10,13,22]tetraoxadiazacyclotetracosine-26,28(27H)-dione, 6,7,9,10,12,13,15,16,18,19-decahydro- (9CI) (CA INDEX NAME)

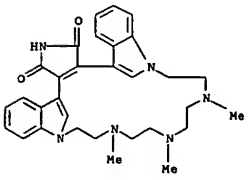


RN 436866-53-4 CAPLUS
CN 5,32:23,28-Dimetheno-29H-dibenzo[q,w]pyrrolo[3,4-t][1,4,7,10,13,16,25]pentaoxadiazacycloheptacosine-29,31(30H)-dione, 6,7,9,10,12,13,15,16,18,19,21,22-dodecahydro- (9CI) (CA INDEX NAME)



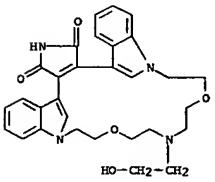
RN 436866-54-5 CAPLUS
CN 5,26:17,22-Dimetheno-9H,23H-dibenzo[k,q]pyrrolo[3,4-n][1,7,4,10,19]dioxatriazacycloheneicosine-23,25(24H)-dione, 11-ethyl-6,7,10,11,12,13,15,16-octahydro- (9CI) (CA INDEX NAME)

L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
CN 6H,23H-5,26:17,22-Dimethenodibenzo[n,t]pyrrolo[3,4-q][1,4,7,10,13]pentaazacycloheneicosine-23,25(24H)-dione, 7,8,9,10,11,12,13,14,15,16-decahydro-8,11,14-trimethyl- (9CI) (CA INDEX NAME)



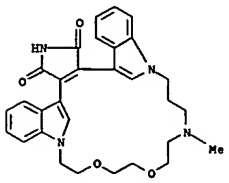
540-472

RN 436866-58-9 CAPLUS
CN 5,26:17,22-Dimetheno-9H,23H-dibenzo[k,q]pyrrolo[3,4-n][1,7,4,10,19]dioxatriazacycloheneicosine-23,25(24H)-dione, 6,7,10,11,12,13,15,16-octahydro-11-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)

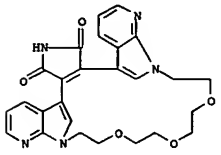


RN 436866-59-0 CAPLUS
CN 5,27:18,23-Dimetheno-24H-dibenzo[l,r]pyrrolo[3,4-o][1,4,7,11,20]dioxatriazacyclododecosine-24,26(25H)-dione, 6,7,9,10,12,13,14,15,16,17-decahydro-14-methyl- (9CI) (CA INDEX NAME)

L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 436866-60-3 CAPLUS
CN 5,26:17,22-Dimetheno-23H-dipyrido[2,3-k:3',2'-q]pyrrolo[3,4-n][1,4,7,10,19]trioxadiazacycloheneicosine-23,25(24H)-dione, 6,7,9,10,12,13,15,16-octahydro- (9CI) (CA INDEX NAME)



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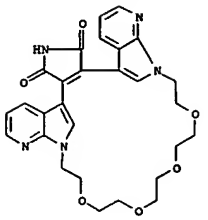
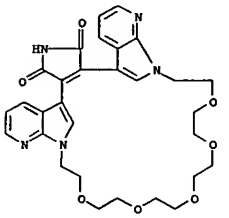
RN 436866-61-4 CAPLUS
CN 5,29:20,25-Dimetheno-26H-dipyrido[2,3-n:3',2'-t]pyrrolo[3,4-q][1,4,7,10,13,22]tetraoxadiazacyclotetracosine-26,28(27H)-dione, 6,7,9,10,12,13,15,16,18,19-decahydro- (9CI) (CA INDEX NAME)

L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

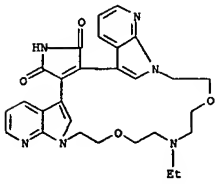


RN 436866-62-5 CAPLUS
CN 5,32:23,28-Dimetheno-29H-dipyrido[2,3-q:3',2'-w]pyrrolo[3,4-t][1,4,7,10,13,16,25]pentaoxadiazacycloheptacosine-29,31(30H)-dione, 6,7,9,10,12,13,15,16,18,19,21,22-dodecahydro- (9CI) (CA INDEX NAME)

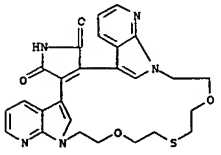


RN 436866-63-6 CAPLUS
CN 5,26:17,22-Dimetheno-9H,23H-dipyrido[2,3-k:3',2'-q]pyrrolo[3,4-n][1,7,4,10,19]dioxatriazacycloheneicosine-23,25(24H)-dione, 11-ethyl-6,7,10,11,12,13,15,16-octahydro- (9CI) (CA INDEX NAME)

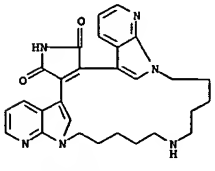
L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 436866-64-7 CAPLUS
CN 5,26:17,22-Dimetheno-23H-dipyrido[2,3-k:3',2'-q]pyrrolo[3,4-n][1,7,4,10,19]dioxathiadiazacycloheneicosine-23,25(24H)-dione, 6,7,9,10,12,13,15,16-octahydro- (9CI) (CA INDEX NAME)

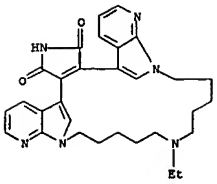


RN 436866-65-8 CAPLUS
CN 6H,23H-5,26:17,22-Dimethenodipyrido[2,3-n:3',2'-t]pyrrolo[3,4-q][1,7,13]triazacycloheneicosine-23,25(24H)-dione, 7,8,9,10,11,12,13,14,15,16-decahydro- (9CI) (CA INDEX NAME)

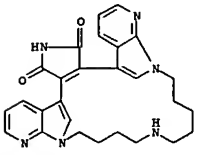


RN 436866-66-9 CAPLUS
CN 6H,23H-5,26:17,22-Dimethenodipyrido[2,3-n:3',2'-t]pyrrolo[3,4-q][1,7,13]triazacycloheneicosine-23,25(24H)-dione, 11-ethyl-7,8,9,10,11,12,13,14,15,16-decahydro- (9CI) (CA INDEX NAME)

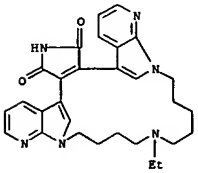
L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 436866-67-0 CAPLUS
CN 5,25:16,21-Dimetheno-22H-dipyrido[2,3-m:3',2'-s]pyrrolo[3,4-p][1,6,12]triazacycloeicosine-22,24(23H)-dione, 6,7,8,9,10,11,12,13,14,15-decahydro- (9CI) (CA INDEX NAME)

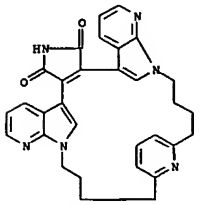


RN 436866-68-1 CAPLUS
CN 5,25:16,21-Dimetheno-22H-dipyrido[2,3-m:3',2'-s]pyrrolo[3,4-p][1,6,12]triazacycloeicosine-22,24(23H)-dione, 10-ethyl-6,7,8,9,10,11,12,13,14,15-decahydro- (9CI) (CA INDEX NAME)

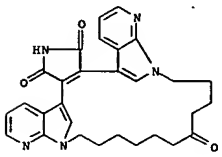


RN 436866-69-2 CAPLUS
CN 25H-5,28:19,24-Dimetheno-10,14-nitrilodipyrido[2,3-b:3',2'-h]pyrrolo[3,4-e][1,10]diazacyclotricosine-25,27(26H)-dione, 6,7,8,9,15,16,17,18-octahydro- (9CI) (CA INDEX NAME)

L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

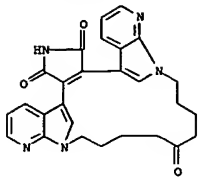


RN 436866-70-5 CAPLUS
CN 6H,23H-5,26:17,22-Dimethenodipyrido[2,3-b:3',2'-h]pyrrolo[3,4-e][1,10]diazacycloheneicosine-10,23,25(7H,24H)-trione, 8,9,11,12,13,14,15,16-octahydro- (9CI) (CA INDEX NAME)



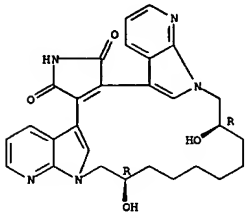
RN 436866-71-6 CAPLUS
CN 6H,21H-5,24:15,20-Dimethenodipyrido[2,3-b:3',2'-h]pyrrolo[3,4-e][1,10]diazacyclononadecine-10,21,23(7H,22H)-trione, 8,9,11,12,13,14-hexahydro- (9CI) (CA INDEX NAME)

L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



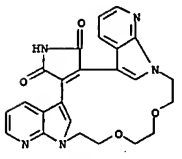
RN 436866-72-7 CAPLUS
CN 5,25:16,21-Dimetheno-22H-dipyrido[2,3-b:3',2'-h]pyrrolo[3,4-e][1,10]diazacycloeicosine-22,24(23H)-dione, 6,7,8,9,10,11,12,13,14,15-decahydro-7,14-dihydroxy-, (7R,14R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

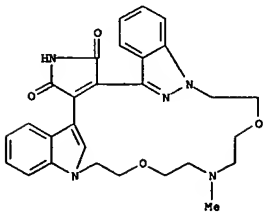


RN 436866-73-8 CAPLUS
CN 5,23:14,19-Dimetheno-20H-dipyrido[2,3-h:3',2'-n]pyrrolo[3,4-k][1,4,7,16]dioxadiazacyclooctadecine-20,22(21H)-dione, 6,7,9,10,12,13-hexahydro- (9CI) (CA INDEX NAME)

L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

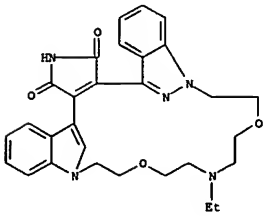


RN 436866-74-9 CAPLUS
CN 17,22-Metheno-5,26-nitrilo-9H,23H-dibenzo[k,q]pyrrolo[3,4-n][1,7,4,10,19]dioxatriazacycloheneicosine-23,25(24H)-dione, 6,7,10,11,12,13,15,16-octahydro-11-methyl- (9CI) (CA INDEX NAME)



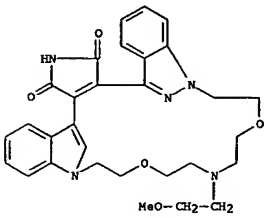
514-403

RN 436866-75-0 CAPLUS
CN 17,22-Metheno-5,26-nitrilo-9H,23H-dibenzo[k,q]pyrrolo[3,4-n][1,7,4,10,19]dioxatriazacycloheneicosine-23,25(24H)-dione, 11-ethyl-6,7,10,11,12,13,15,16-octahydro- (9CI) (CA INDEX NAME)

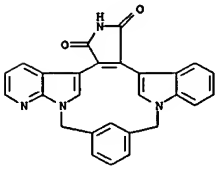


L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

RN 436866-76-1 CAPLUS
CN 17,22-Metheno-5,26-nitrilo-9H,23H-dibenzo[k,q]pyrrolo[3,4-n][1,7,4,10,19]dioxatriazacycloheneicosine-23,25(24H)-dione, 6,7,10,11,12,13,15,16-octahydro-11-(2-methoxyethyl)- (9CI) (CA INDEX NAME)

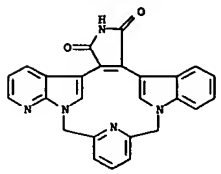


RN 436866-77-2 CAPLUS
CN 6H,12H,19H-5,22:7,11:13,18-Trimethenopyrido[2,3-j]pyrrolo[3,4-m][1,9]benzodiazacycloheptadecine-19,21(20H)-dione (9CI) (CA INDEX NAME)

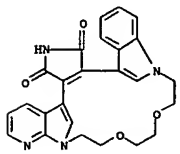


RN 436866-78-3 CAPLUS
CN 6H,12H,19H-5,22:13,18-Dimetheno-7,11-nitrilopyrido[2,3-j]pyrrolo[3,4-m][1,9]benzodiazacycloheptadecine-19,21(20H)-dione (9CI) (CA INDEX NAME)

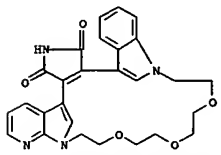
L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 436866-79-4 CAPLUS
CN 5,23:14,19-Dimetheno-20H-pyrido[2,3-k]pyrrolo[3,4-n][4,7,1,10]benzodioxadiazacyclooctadecine-20,22(21H)-dione, 6,7,9,10,12,13-hexahydro- (9CI) (CA INDEX NAME)

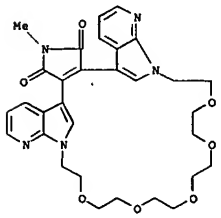


RN 436866-80-7 CAPLUS
CN 5,26:17,22-Dimetheno-23H-pyrido[2,3-n]pyrrolo[3,4-q][4,7,10,1,13]benzotrioxadiazacycloheneicosine-23,25(24H)-dione, 6,7,9,10,12,13,15,16-octahydro- (9CI) (CA INDEX NAME)

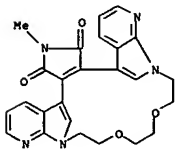


IT 436866-83-0P 436866-85-2P 436866-87-4P
436866-89-6P 436866-90-9P 436866-92-1P

L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
RN 436866-87-4 CAPLUS
CN 5,32:23,28-Dimetheno-29H-dipyrido[2,3-q:3',2'-w]pyrrolo[3,4-t][1,4,7,10,13,16,25]pentaoxadiazacycloheptacosine-29,31(30H)-dione, 6,7,9,10,12,13,15,16,18,19,21,22-dodecahydro-30-methyl- (9CI) (CA INDEX NAME)

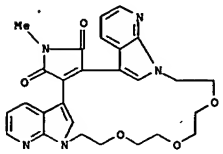


RN 436866-89-6 CAPLUS
CN 5,23:14,19-Dimetheno-20H-dipyrido[2,3-h:3',2'-n]pyrrolo[3,4-k][1,4,7,16]dioxadiazacyclooctadecine-20,22(21H)-dione, 6,7,9,10,12,13-hexahydro-21-methyl- (9CI) (CA INDEX NAME)

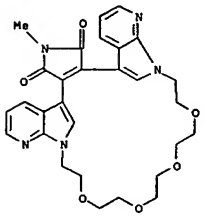


RN 436866-90-9 CAPLUS
CN 5,23:14,19-Dimetheno-20H-dibenzo[h,n]pyrrolo[3,4-k][1,4,7,16]dioxadiazacyclooctadecine-20,22(21H)-dione, 6,7,9,10,12,13-hexahydro-21-methyl- (9CI) (CA INDEX NAME)

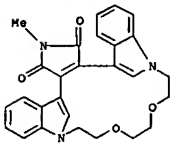
L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
436866-94-3P 436866-96-5P 436866-98-7P
436867-00-4P 436867-02-6P 436867-04-8P
436867-07-1P 436867-09-3P 436867-16-2P
436867-18-4P 436867-19-5P 436867-20-8P
436867-21-9P 436867-26-4P 436867-27-5P
436867-28-6P 436867-32-2P 436867-38-8P
436867-41-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of bis(heterocyclyl)pyrrolinones and bis(heterocyclyl)pyrrolediones as inhibitors of kinases for the treatment of kinase-mediated diseases such as diabetes, stroke, transplant rejection, psoriasis, and baldness)
RN 436866-83-0 CAPLUS
CN 5,26:17,22-Dimetheno-23H-dipyrido[2,3-k:3',2'-q]pyrrolo[3,4-n][1,4,7,10,19]trioxadiazacycloheneicosine-23,25(24H)-dione, 6,7,9,10,12,13,15,16-octahydro-24-methyl- (9CI) (CA INDEX NAME)



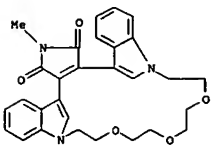
RN 436866-85-2 CAPLUS
CN 5,29:20,25-Dimetheno-26H-dipyrido[2,3-n:3',2'-t]pyrrolo[3,4-q][1,4,7,10,13,22]tetraoxadiazacyclotetracosine-26,28(27H)-dione, 6,7,9,10,12,13,15,16,18,19-decahydro-27-methyl- (9CI) (CA INDEX NAME)



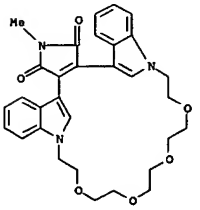
L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 436866-92-1 CAPLUS
CN 5,26:17,22-Dimetheno-23H-dibenzo[k,q]pyrrolo[3,4-n][1,4,7,10,19]trioxadiazacycloheneicosine-23,25(24H)-dione, 6,7,9,10,12,13,15,16-octahydro-24-methyl- (9CI) (CA INDEX NAME)

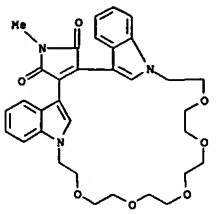


RN 436866-94-3 CAPLUS
CN 5,29:20,25-Dimetheno-26H-dibenzo[n,t]pyrrolo[3,4-q][1,4,7,10,13,22]tetraoxadiazacyclotetracosine-26,28(27H)-dione, 6,7,9,10,12,13,15,16,18,19-decahydro-27-methyl- (9CI) (CA INDEX NAME)

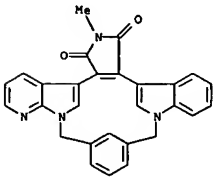


RN 436866-96-5 CAPLUS
CN 5,32:23,28-Dimetheno-29H-dibenzo[q,w]pyrrolo[3,4-t][1,4,7,10,13,16,25]pentaoxadiazacycloheptacosine-29,31(30H)-dione, 6,7,9,10,12,13,15,16,18,19,21,22-dodecahydro-30-methyl- (9CI) (CA INDEX NAME)

L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

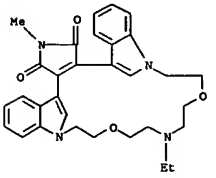


RN 436866-98-7 CAPLUS
CN 6H,12H,19H-5,22:7,11:13,18-Trimethenopyrido[2,3-j]pyrrolo[3,4-m][1,9]benzodiazacycloheptadecine-19,21(20H)-dione, 20-methyl- (9CI) (CA INDEX NAME)

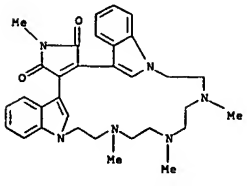


RN 436867-00-4 CAPLUS
CN 6H,12H,19H-5,22:13,18-Dimetheno-7,11-nitrilopyrido[2,3-j]pyrrolo[3,4-m][1,9]benzodiazacycloheptadecine-19,21(20H)-dione, 20-methyl- (9CI) (CA INDEX NAME)

L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
11-ethyl-6,7,10,11,12,13,15,16-octahydro-24-methyl- (9CI) (CA INDEX NAME)

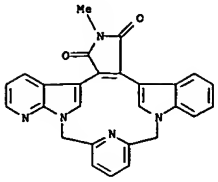


RN 436867-09-3 CAPLUS
CN 6H,23H-5,26:17,22-Dimethenodibenzo[n,t]pyrrolo[3,4-q][1,4,7,10,13]pentaazacycloheneicosine-23,25(24H)-dione, 7,8,9,10,11,12,13,14,15,16-decahydro-8,11,14,24-tetramethyl- (9CI) (CA INDEX NAME)

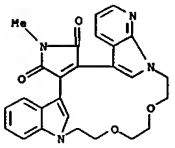


RN 436867-16-2 CAPLUS
CN 5,26:17,22-Dimetheno-9H,23H-dipyrido[2,3-k:3',2'-q]pyrrolo[3,4-n][1,7,4,10,19]dioxatriazacycloheneicosine-23,25(24H)-dione, 11-ethyl-6,7,10,11,12,13,15,16-octahydro-24-methyl- (9CI) (CA INDEX NAME)

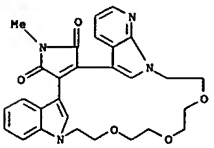
L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 436867-02-6 CAPLUS
CN 5,23:14,19-Dimetheno-20H-pyrido[2,3-k]pyrrolo[3,4-n][4,7,1,10]benzodioxadiazacyclooctadecine-20,22(21H)-dione, 6,7,9,10,12,13-hexahydro-21-methyl- (9CI) (CA INDEX NAME)

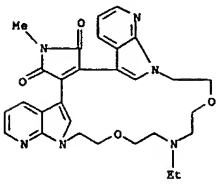


RN 436867-04-8 CAPLUS
CN 5,26:17,22-Dimetheno-23H-pyrido[2,3-n]pyrrolo[3,4-q][4,7,10,1,13]benzotrioxadiazacycloheneicosine-23,25(24H)-dione, 6,7,9,10,12,13,15,16-octahydro-24-methyl- (9CI) (CA INDEX NAME)

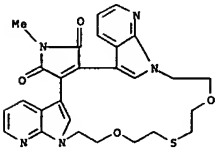


RN 436867-07-1 CAPLUS
CN 5,26:17,22-Dimetheno-9H,23H-dibenzo[k,q]pyrrolo[3,4-n][1,7,4,10,19]dioxatriazacycloheneicosine-23,25(24H)-dione,

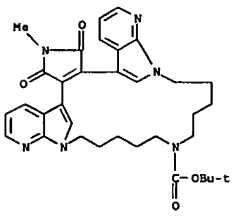
L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



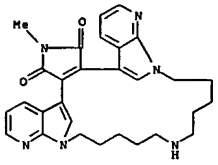
RN 436867-18-4 CAPLUS
CN 5,26:17,22-Dimetheno-23H-dipyrido[2,3-k:3',2'-q]pyrrolo[3,4-n][1,7,4,10,19]dioxathiadiazacycloheneicosine-23,25(24H)-dione, 6,7,9,10,12,13,15,16-octahydro-24-methyl- (9CI) (CA INDEX NAME)



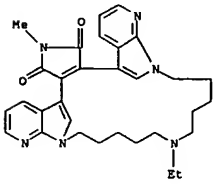
RN 436867-19-5 CAPLUS
CN 6H,23H-5,26:17,22-Dimethenodipyrido[2,3-n:3',2'-t]pyrrolo[3,4-q][1,7,13]triazacycloheneicosine-11(12H)-carboxylic acid, 7,8,9,10,13,14,15,16,24,25-decahydro-24-methyl-23,25-dioxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
RN 436867-20-8 CAPLUS
CN 6H,23H-5,26:17,22-Dimethenodipyrido[2,3-n:3',2'-t]pyrrolo[3,4-q][1,7,13]triazacycloheneicosine-23,25(24H)-dione, 7,8,9,10,11,12,13,14,15,16-decahydro-24-methyl- (9CI) (CA INDEX NAME)

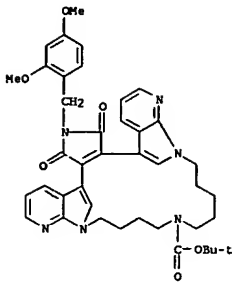


RN 436867-21-9 CAPLUS
CN 6H,23H-5,26:17,22-Dimethenodipyrido[2,3-n:3',2'-t]pyrrolo[3,4-q][1,7,13]triazacycloheneicosine-23,25(24H)-dione, 11-ethyl-7,8,9,10,11,12,13,14,15,16-decahydro-24-methyl- (9CI) (CA INDEX NAME)

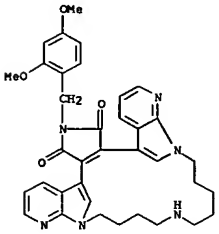


RN 436867-26-4 CAPLUS
CN 5,25:16,21-Dimetheno-22H-dipyrido[2,3-m:3',2'-s]pyrrolo[3,4-p][1,6,12]triazacycloeicosine-10(11H)-carboxylic acid, 23-[(2,4-dimethoxyphenyl)methyl]-6,7,8,9,12,13,14,15,23,24-decahydro-22,24-dioxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

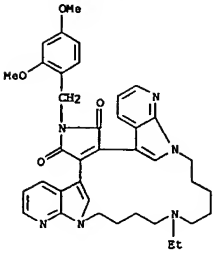


RN 436867-27-5 CAPLUS
CN 5,25:16,21-Dimetheno-22H-dipyrido[2,3-m:3',2'-s]pyrrolo[3,4-p][1,6,12]triazacycloeicosine-22,24(23H)-dione, 23-[(2,4-dimethoxyphenyl)methyl]-6,7,8,9,10,11,12,13,14,15-decahydro- (9CI) (CA INDEX NAME)

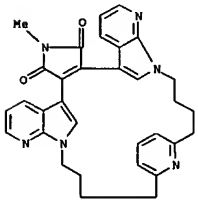


RN 436867-28-6 CAPLUS
CN 5,25:16,21-Dimetheno-22H-dipyrido[2,3-m:3',2'-s]pyrrolo[3,4-p][1,6,12]triazacycloeicosine-22,24(23H)-dione, 23-[(2,4-dimethoxyphenyl)methyl]-10-ethyl-6,7,8,9,10,11,12,13,14,15-decahydro- (9CI) (CA INDEX NAME)

L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

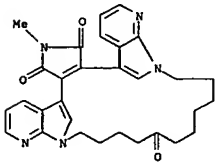


RN 436867-32-2 CAPLUS
CN 25H-5,28:19,24-Dimetheno-10,14-nitrilodipyrido[2,3-b:3',2'-h]pyrrolo[3,4-e][1,10]diazacyclotricosine-25,27(26H)-dione, 6,7,8,9,15,16,17,18-octahydro-26-methyl- (9CI) (CA INDEX NAME)



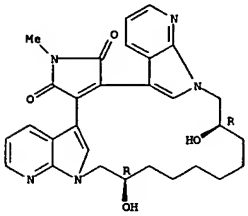
RN 436867-38-8 CAPLUS
CN 6H,23H-5,26:17,22-Dimethenodipyrido[2,3-b:3',2'-h]pyrrolo[3,4-e][1,10]diazacycloheneicosine-10,23,25(7H,24H)-trione, 8,9,11,12,13,14,15,16-octahydro-24-methyl- (9CI) (CA INDEX NAME)

L53 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 436867-41-3 CAPLUS
CN 5,25:16,21-Dimetheno-22H-dipyrido[2,3-b:3',2'-h]pyrrolo[3,4-e][1,10]diazacycloeicosine-22,24(23H)-dione, 6,7,8,9,10,11,12,13,14,15-decahydro-7,14-dihydroxy-23-methyl-, (7R,14R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

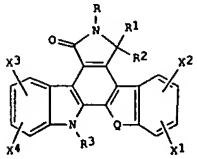


REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 3 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:293663 CAPLUS
DOCUMENT NUMBER: 136:279651
TITLE: Preparation and biological activity of indolopyrrolocarbazoledione anhydro glycosides as topoisomerase inhibitors
INVENTOR(S): Ruediger, Edward H.; Frennesson, David B.; Mahler, Mikael; Zimmermann, Kurt
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA; Saulnier, Mark, G.; Balasubramanian, Neekakantan
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030942	A2	20020418	WO 2001-US30641	20011001
WO 2002030942	A3	20021003		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002111375	A1	20020815	US 2001-965069	20010927
US 6610727	B2	20030826		
EP 1326876	A2	20030716	EP 2001-979347	20011001
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-238696P P 20001006
WO 2001-US30641 W 20011001
OTHER SOURCE(S): MARPAT 136:279651
GI

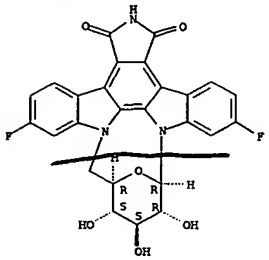


I

AB The present invention concerns novel sugar derivs. of indolocarbazole

L53 ANSWER 3 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
glycosides I wherein R is H, OH, acyl, NH2, alkylamine, alkyl; R1 and R2 independently H, OH; R1R2 together are O; X1-X4 are independently H, halogen, cyano, ether, CF3, alkylcarbonyl, alkyl, nitro, alkoxyaminoalkyl, amine, thiol, ester, and pharmaceutical formulations thereof which exhibit topoisomerase-I activity and are useful in inhibiting the proliferation of tumor cells. Thus, 3,9-Difluoro-12,13-dihydro-13-[(3,6-anhydro)-.alpha.-D-glucopyranosyl]-5H-indolo[2,3-a]pyrrolo[3,4-c]carbazole-5,7(6H)-dione was prepd. and tested in vitro as human topoisomerase I inhibitor (EC50 = 0.36 .mu.M) and as antitumor agent against murine P388 cell line (IC50 = 0.0388.mu.M).
IT 406722-28-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and biol. activity of indolopyrrolocarbazoledione anhydro glycosides as topoisomerase inhibitors)
RN 406722-28-9 CAPLUS
CN 9,13-Epoxy-1H-diindolo[1,2,3-hi:3',2',1'-mn]pyrrolo[3,4-k][1,8]benzodiazecine-1,3(2H)-dione, 6,17-difluoro-9,10,11,12,13,14-hexahydro-10,11,12-trihydroxy-, (9R,10R,11S,12S,13R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L53 ANSWER 4 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:293662 CAPLUS
DOCUMENT NUMBER: 136:295021
TITLE: Preparation and biological activity of indolopyrrolocarbazoledione glycosides as topoisomerase inhibitors
INVENTOR(S): Saulnier, Mark G.; Ruediger, Edward H.; Balasubramanian, Neekakantan; Mahler, Mikael; Beaulieu, Francis; Bachand, Carol; Frennesson, David B.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030941	A2	20020418	WO 2001-US30640	20011001
WO 2002030941	A3	20021003		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002107237	A1	20020808	US 2001-965976	20010927
AU 2001096435	A5	20020422	AU 2001-96435	20011001
EP 1326874	A2	20030716	EP 2001-977305	20011001
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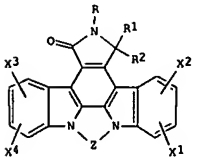
PRIORITY APPLN. INFO.: US 2000-238726P P 20001006
WO 2001-US30640 W 20011001
OTHER SOURCE(S): MARPAT 136:295021
GI

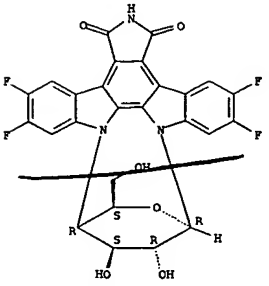


I

AB The present invention relates to novel N12, N13-bridged sugar derivs. of indolylopyrrolocarbazoles I wherein Z is a pyranose or furanose; R is H, OH, acyl, NH2, alkylamine, alkyl; R1 and R2 independently H, OH; R1R2 together are O; X1-X4 are independently H, halogen, cyano, ether, CF3,

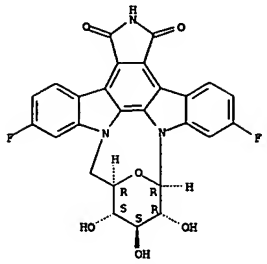
L53 ANSWER 4 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
alkylcarbonyl, alkyl, nitro, alkoxyaminoalkyl, amine, thiol, ester, and pharmaceutical formulations thereof which exhibit topoisomerase-I activity and are useful in inhibiting the proliferation of tumor cells. Thus, 2,3,9,10-tetrafluoro-12,13-(1,6-.beta.-D-glucopyranosyl)-6,7,12,13-tetrahydro(5H)indolo[2,3-a]pyrrolo[3,4-c]carbazole-5,7-dione was prepd. and tested in vitro as human topoisomerase inhibitor (EC50 = 0.35 .mu.M) and as antitumor agent against murine P388 cell line (IC50 = 0.05.mu.M).
IT 406913-52-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. and biol. activity of indolopyrrolocarbazoledione glycosides as topoisomerase inhibitors)
RN 406913-52-8 CAPLUS
CN 9,12-Ethano-1H,9H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][3,1,6]benzoxadiazocine-1,3(2H)-dione, 5,6,15,16-tetrafluoro-11,12-dihydro-18,19-dihydroxy-11-(hydroxymethyl)-, (9R,11S,12R,18S,19R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



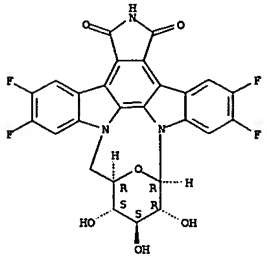
IT 406722-28-9P 406913-42-6P 406913-43-7P
406913-44-8P 406913-45-9P 406913-46-0P
406913-47-1P 406913-48-2P 406913-55-1P
406913-66-4P 406913-69-7P 406913-71-1P
406913-73-3P 406913-74-4P 406913-94-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and biol. activity of indolopyrrolocarbazoledione glycosides as topoisomerase inhibitors)
RN 406722-28-9 CAPLUS
CN 9,13-Epoxy-1H-diindolo[1,2,3-hi:3',2',1'-mn]pyrrolo[3,4-k][1,8]benzodiazecine-1,3(2H)-dione, 6,17-difluoro-9,10,11,12,13,14-hexahydro-10,11,12-trihydroxy-, (9R,10R,11S,12S,13R)- (9CI) (CA INDEX NAME)

L53 ANSWER 4 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
Absolute stereochemistry.



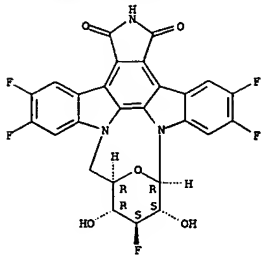
RN 406913-42-6 CAPLUS
CN 9,13-Epoxy-1H-diindolo[1,2,3-hi:3',2',1'-mn]pyrrolo[3,4-k][1,8]benzodiazecine-1,3(2H)-dione, 5,6,17,18-tetrafluoro-9,10,11,12,13,14-hexahydro-10,11,12-trihydroxy-, (9R,10R,11S,12S,13R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



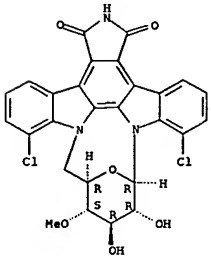
RN 406913-43-7 CAPLUS
CN 9,13-Epoxy-1H-diindolo[1,2,3-hi:3',2',1'-mn]pyrrolo[3,4-k][1,8]benzodiazecine-1,3(2H)-dione, 5,6,17,18-tetrafluoro-9,10,11,12,13,14-hexahydro-10,11-dihydroxy-, (9R,10R,11S,13S)- (9CI) (CA INDEX NAME)

L53 ANSWER 4 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
Absolute stereochemistry.



RN 406913-46-0 CAPLUS
CN 9,13-Epoxy-1H-diindolo[1,2,3-hi:3',2',1'-mn]pyrrolo[3,4-k][1,8]benzodiazecine-1,3(2H)-dione, 7,16-dichloro-9,10,11,12,13,14-hexahydro-10,11-dihydroxy-12-methoxy-, (9R,10R,11R,12S,13R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

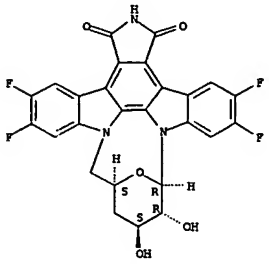


RN 406913-47-1 CAPLUS
CN 9,13-Epoxy-1H-diindolo[1,2,3-hi:3',2',1'-mn]pyrrolo[3,4-k][1,8]benzodiazecine-1,3(2H)-dione, 5,6,11,12,17,18-hexafluoro-9,10,11,12,13,14-hexahydro-10-hydroxy-, (9R,10S,11R,12R,13R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

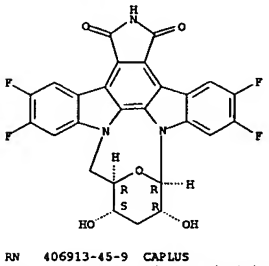
L53 ANSWER 4 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

Absolute stereochemistry.



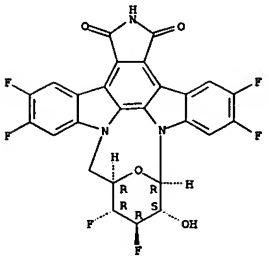
RN 406913-44-8 CAPLUS
CN 9,13-Epoxy-1H-diindolo[1,2,3-hi:3',2',1'-mn]pyrrolo[3,4-k][1,8]benzodiazecine-1,3(2H)-dione, 5,6,17,18-tetrafluoro-9,10,11,12,13,14-hexahydro-10,12-dihydroxy-, (9R,10R,12S,13R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



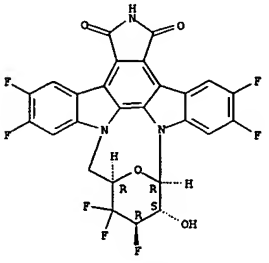
RN 406913-45-9 CAPLUS
CN 9,13-Epoxy-1H-diindolo[1,2,3-hi:3',2',1'-mn]pyrrolo[3,4-k][1,8]benzodiazecine-1,3(2H)-dione, 5,6,11,17,18-pentafluoro-9,10,11,12,13,14-hexahydro-10,12-dihydroxy-, (9R,10S,11S,12R,13R)- (9CI) (CA INDEX NAME)

L53 ANSWER 4 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 406913-48-2 CAPLUS
CN 9,13-Epoxy-1H-diindolo[1,2,3-hi:3',2',1'-mn]pyrrolo[3,4-k][1,8]benzodiazecine-1,3(2H)-dione, 5,6,11,12,12,17,18-heptafluoro-9,10,11,12,13,14-hexahydro-10-hydroxy-, (9R,10S,11R,13R)- (9CI) (CA INDEX NAME)

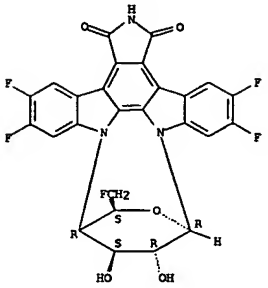
Absolute stereochemistry.



RN 406913-55-1 CAPLUS
CN 9,12-Ethano-1H,9H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][3,1,6]benzoxadiazocine-1,3(2H)-dione, 5,6,15,16-tetrafluoro-11-(fluoromethyl)-11,12-dihydro-18,19-dihydroxy-, (9R,11S,12R,18S,19R)- (9CI) (CA INDEX NAME)

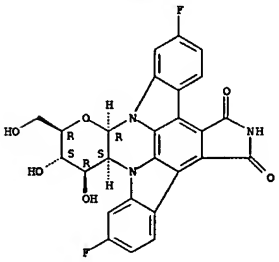
Absolute stereochemistry.

L53 ANSWER 4 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



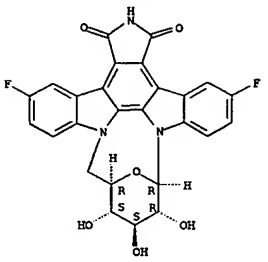
RN 406913-66-4 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 3,12-difluoro-5a,8,9,9a-tetrahydro-8,9-dihydroxy-7-(hydroxymethyl)-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



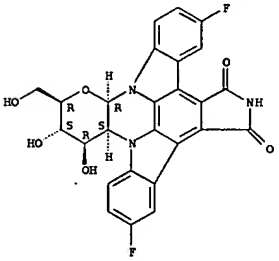
RN 406913-69-7 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 2,13-difluoro-5a,8,9,9a-tetrahydro-8,9-dihydroxy-7-(hydroxymethyl)-, (5aR,7R,8R,9R,9aS)- (9CI) (CA INDEX NAME)

L53 ANSWER 4 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
Absolute stereochemistry.



RN 406913-74-4 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 2,13-difluoro-5a,8,9,9a-tetrahydro-8,9-dihydroxy-7-(hydroxymethyl)-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

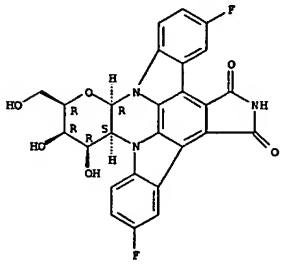
Absolute stereochemistry.



RN 406913-94-8 CAPLUS
CN 9,13-Epoxy-1H-diindolo[1,2,3-hi:3',2',1'-mn]pyrrolo[3,4-k][1,8]benzodiazecine-1,3(2H)-dione, 6,12,17-trifluoro-9,10,11,12,13,14-hexahydro-10,11-dihydroxy-, (9R,10R,11R,12S,13R)- (9CI) (CA INDEX NAME)

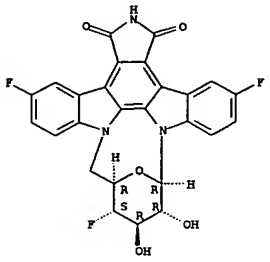
Absolute stereochemistry.

L53 ANSWER 4 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
Absolute stereochemistry.



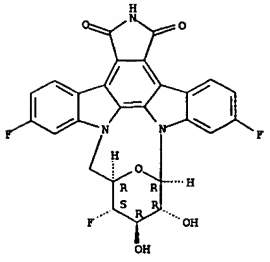
RN 406913-71-1 CAPLUS
CN 9,13-Epoxy-1H-diindolo[1,2,3-hi:3',2',1'-mn]pyrrolo[3,4-k][1,8]benzodiazecine-1,3(2H)-dione, 5,12,18-trifluoro-9,10,11,12,13,14-hexahydro-10,11-dihydroxy-, (9R,10R,11R,12S,13R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 406913-73-3 CAPLUS
CN 9,13-Epoxy-1H-diindolo[1,2,3-hi:3',2',1'-mn]pyrrolo[3,4-k][1,8]benzodiazecine-1,3(2H)-dione, 5,18-difluoro-9,10,11,12,13,14-hexahydro-10,11,12-trihydroxy-, (9R,10R,11S,12S,13R)- (9CI) (CA INDEX NAME)

L53 ANSWER 4 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



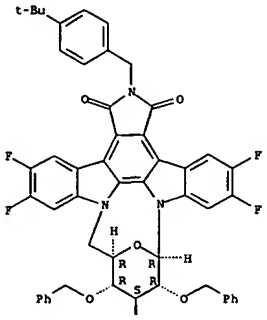
IT 406913-39-1P 406913-41-5P 406913-50-6P
406913-53-9P 406913-54-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and biol. activity of indolopyrrolocarbazoledione glycosides as topoisomerase inhibitors)

RN 406913-39-1 CAPLUS
CN 9,13-Epoxy-1H-diindolo[1,2,3-hi:3',2',1'-mn]pyrrolo[3,4-k][1,8]benzodiazecine-1,3(2H)-dione, 2-[[4-(1,1-dimethylethyl)phenyl]methyl]-5,6,17,18-tetrafluoro-9,10,11,12,13,14-hexahydro-10,11,12-tris(phenylmethoxy)-, (9R,10R,11S,12R,13R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L53 ANSWER 4 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-A

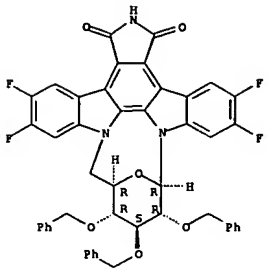


PAGE 2-A

RN 406913-41-5 CAPLUS
CN 9,13-Epoxy-1H-diindolo[1,2,3-hi:3',2',1'-mn]pyrrolo[3,4-k][1,8]benzodiazecine-1,3(2H)-dione, 5,6,17,18-tetrafluoro-9,10,11,12,13,14-hexahydro-10,11,12-tris(phenylmethoxy)-, (9R,10R,11S,12R,13R)- (9CI) (CA INDEX NAME)

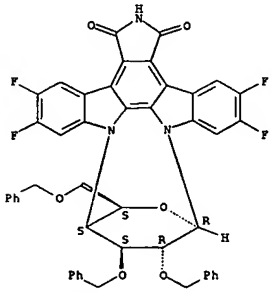
Absolute stereochemistry.

L53 ANSWER 4 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 406913-50-6 CAPLUS
CN 9,12-Ethano-1H,9H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][3,1,6]benzoxadiazocine-1,3(2H)-dione, 5,6,15,16-tetrafluoro-11,12-dihydro-18,19-bis(phenylmethoxy)-11-[(phenylmethoxy)methyl]-, (9R,11S,12S,18S,19R)- (9CI) (CA INDEX NAME)

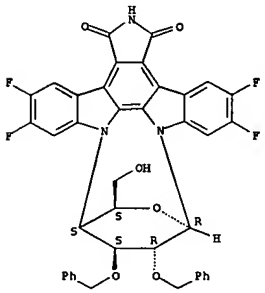
Absolute stereochemistry.



RN 406913-53-9 CAPLUS
CN 9,12-Ethano-1H,9H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-

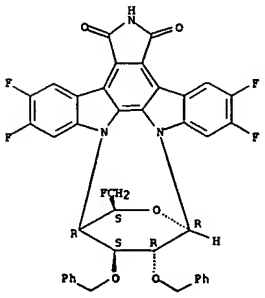
L53 ANSWER 4 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
i][3,1,6]benzoxadiazocine-1,3(2H)-dione, 5,6,15,16-tetrafluoro-11,12-dihydro-11-(hydroxymethyl)-18,19-bis(phenylmethoxy)-, (9R,11S,12S,18S,19R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 406913-54-0 CAPLUS
CN 9,12-Ethano-1H,9H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][3,1,6]benzoxadiazocine-1,3(2H)-dione, 5,6,15,16-tetrafluoro-11-(fluoromethyl)-11,12-dihydro-18,19-bis(phenylmethoxy)-, (9R,11S,12R,18S,19R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L53 ANSWER 4 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

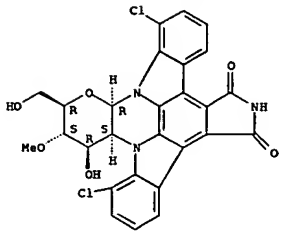
L53 ANSWER 5 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:112624 CAPLUS
DOCUMENT NUMBER: 136:263351
TITLE: Syntheses and Antiproliferative Activities of New Rebeccamycin Derivatives with the Sugar Unit Linked to Both Indole Nitrogens
AUTHOR(S): Marminon, Christelle; Anizon, Fabrice; Moreau, Pascale; Leonce, Stephane; Pierre, Alain; Pfeiffer, Bruno; Renard, Pierre; Prudhomme, Michelle
CORPORATE SOURCE: Synthese et Etude de Systemes a Interet Biologique, Universite Blaise Pascal UMR 6504, Aubiere, 63177, Fr.
SOURCE: Journal of Medicinal Chemistry (2002), 45(6), 1330-1339
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The synthesis of new rebeccamycin derivs., in which the carbohydrate moiety is attached to both indole nitrogens, is described. The newly synthesized compds. were tested for their abilities to block the cell cycle of murine leukemia L1210 cells and their in vitro antiproliferative activities against four tumor cell lines (murine L1210 leukemia and human HT29 colon carcinoma, A549 non-small-cell lung carcinoma, K-562 leukemia). Their biol. activities are compared with those of the parent compd. rebeccamycin. Some of the new compds. exhibit potent antiproliferative activities, either against the four cell lines or mostly the two leukemias (L1210 and K-562 cell lines). The 3,9-diformyl analog 9 was selective toward L1210 cells, whereas the 3,9-dibromo 16 was strongly cytotoxic toward the four cell lines tested. Nonselective compd. 16 and 3,9-dinitro 13, which exhibited selectivity toward leukemia tumor cell lines, were selected for in-depth evaluation, including in vivo expts.

IT **340162-37-0**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(syntheses and antiproliferative activities of rebeccamycin derivs. with the sugar unit linked to both indole nitrogens)
RN 340162-37-0 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 4,11-dichloro-5a,8,9,9a-tetrahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

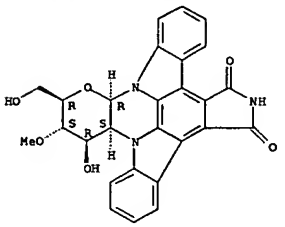
Absolute stereochemistry.

L53 ANSWER 5 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



IT **340162-38-1**
RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(syntheses and antiproliferative activities of rebeccamycin derivs. with the sugar unit linked to both indole nitrogens)
RN 340162-38-1 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 5a,8,9,9a-tetrahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

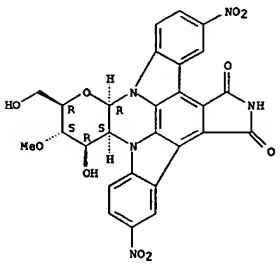
Absolute stereochemistry.



IT **340162-49-4P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(syntheses and antiproliferative activities of rebeccamycin derivs. with the sugar unit linked to both indole nitrogens)

L53 ANSWER 5 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
RN 340162-49-4 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 5a,8,9,9a-tetrahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-2,13-dinitro-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

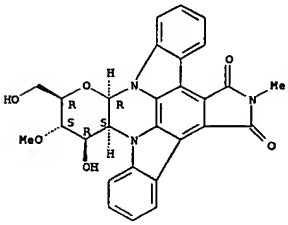
Absolute stereochemistry.



IT **340162-40-5P 340162-41-6P 340162-43-8P**
340162-45-0P 340162-47-2P 340162-50-7P
340162-51-8P 340162-52-9P 340162-53-0P
340162-54-1P 340162-55-2P 340162-56-3P
340162-60-9P 340162-70-1P 340162-71-2P
405265-19-2P 405265-21-6P 405265-22-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(syntheses and antiproliferative activities of rebeccamycin derivs. with the sugar unit linked to both indole nitrogens)
RN 340162-40-5 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 5a,8,9,9a-tetrahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-16-methyl-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

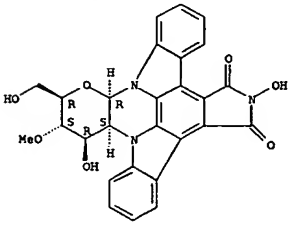
Absolute stereochemistry.

L53 ANSWER 5 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 340162-41-6 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 5a,8,9,9a-tetrahydro-9,16-dihydroxy-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

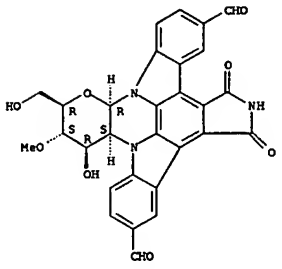
Absolute stereochemistry.



RN 340162-43-8 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-2,13-dicarboxaldehyde, 5a,8,9,9a,16,17-hexahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-15,17-dioxo-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

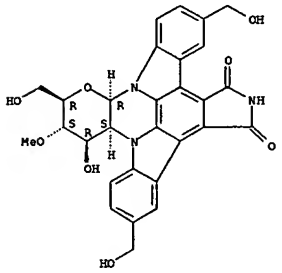
Absolute stereochemistry.

L53 ANSWER 5 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 340162-45-0 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 5a,8,9,9a-tetrahydro-9-hydroxy-2,7,13-tris(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



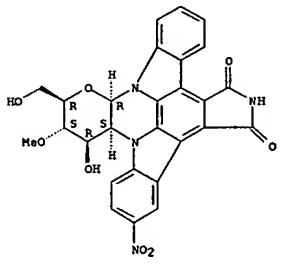
RN 340162-47-2 CAPLUS
CN 7,10-Methano-10H,16H-[1,4]dioxepino[5,6-b]diindolo[1,2,3-de:3',2',1'-ij]pyrrolo[3,4-g]quinoxaline-16,18(17H)-dione, 5a,7,8,10a-tetrahydro-19-methoxy-, (5aR,7R,10R,10aS,19S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L53 ANSWER 5 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

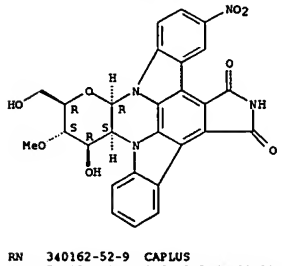
RN 340162-50-7 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 5a,8,9,9a-tetrahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-13-nitro-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 340162-51-8 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 5a,8,9,9a-tetrahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-2-nitro-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 340162-52-9 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 2,13-diamino-5a,8,9,9a-tetrahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

L53 ANSWER 5 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

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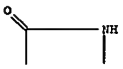

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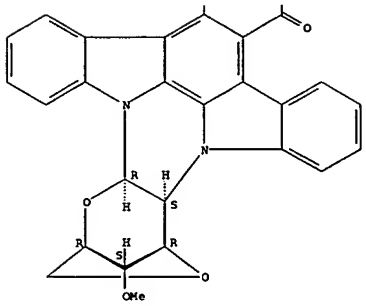
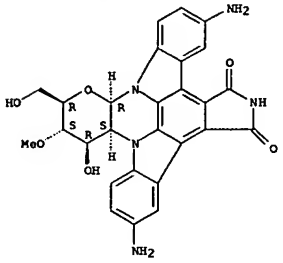


L53 ANSWER 5 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

Absolute stereochemistry.



RN 340162-53-0 CAPLUS
CN 7,10-Methano-10H,16H-[1,4]dioxepino[5,6-b]diindolo[1,2,3-de:3',2',1'-ij]pyrrolo[3,4-g]quinoxaline-16,18(17H)-dione, 5a,7,8,10a-tetrahydro-19-methoxy-2,14-dinitro-, (5aR,7R,10R,10aS,19S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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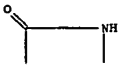

L53 ANSWER 5 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

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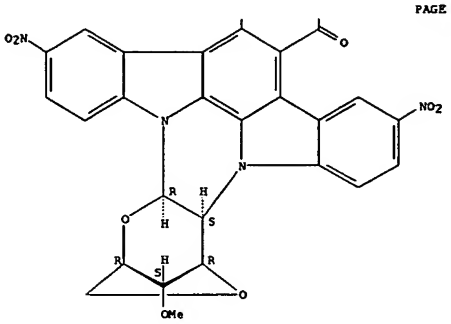

RN 340162-54-1 CAPLUS
CN 7,10-Methano-10H,16H-[1,4]dioxepino[5,6-b]diindolo[1,2,3-de:3',2',1'-ij]pyrrolo[3,4-g]quinoxaline-16,18(17H)-dione, 5a,7,8,10a-tetrahydro-19-methoxy-14-nitro-, (5aR,7R,10R,10aS,19S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L53 ANSWER 5 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

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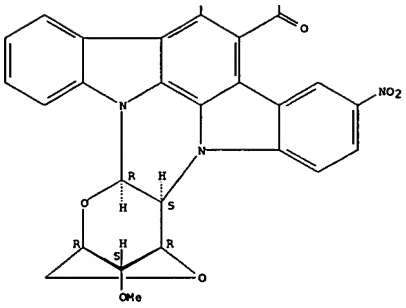
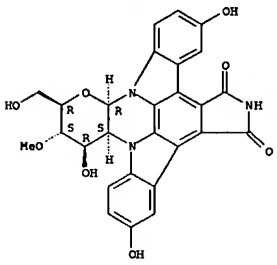


L53 ANSWER 5 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

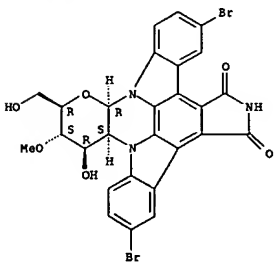
RN 340162-55-2 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 5a,8,9,9a-tetrahydro-2,9,13-trihydroxy-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 340162-56-3 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 2,13-dibromo-5a,8,9,9a-tetrahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

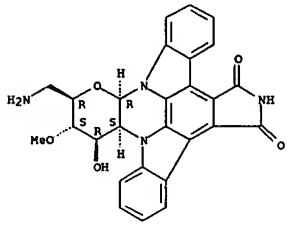
Absolute stereochemistry.



RN 340162-60-9 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 7-(aminomethyl)-5a,8,9,9a-tetrahydro-9-hydroxy-8-methoxy-, monohydrochloride, (5aR,7R,8S,9R,9aS)- (9CI) (CA

L53 ANSWER 5 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
INDEX NAME)

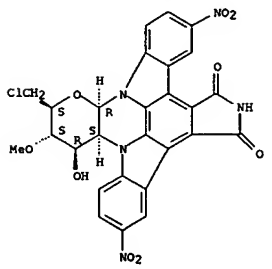
Absolute stereochemistry.



● HCl

RN 340162-70-1 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 7-(chloromethyl)-5a,8,9,9a-tetrahydro-9-hydroxy-8-methoxy-2,13-dinitro-, (5aR,7S,8S,9R,9aS)- (9CI) (CA INDEX NAME)

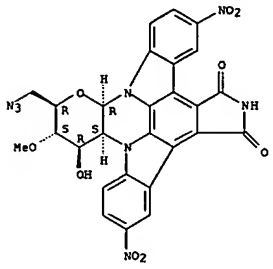
Absolute stereochemistry.



RN 340162-71-2 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 7-(azidomethyl)-5a,8,9,9a-tetrahydro-9-hydroxy-8-methoxy-2,13-dinitro-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX

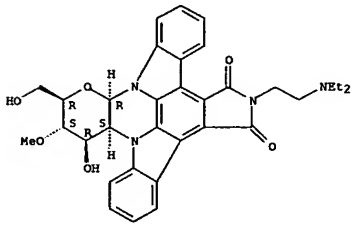
L53 ANSWER 5 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
NAME)

Absolute stereochemistry.



RN 405265-19-2 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 16-[2-(diethylamino)ethyl]-5a,8,9,9a-tetrahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 405265-21-6 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 9-(acetyloxy)-7-(azidomethyl)-5a,8,9,9a-tetrahydro-8-methoxy-2,13-dinitro-, (5aR,7R,8R,9R,9aS)- (9CI) (CA INDEX

L53 ANSWER 5 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

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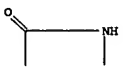

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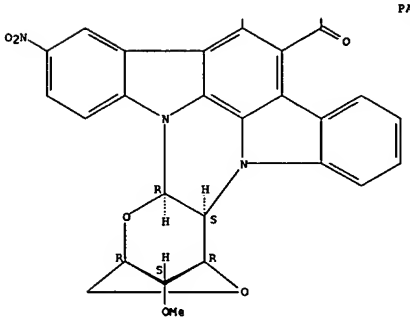
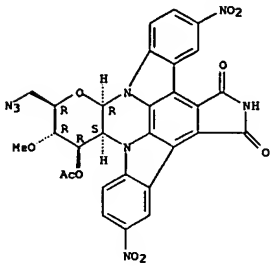


IT 340162-42-7P 340162-44-9P 340162-46-1P
340162-48-3P 340162-66-5P 340162-67-6P
340162-68-7P 405265-20-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

L53 ANSWER 5 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
NAME)

Absolute stereochemistry.



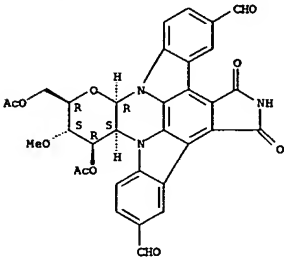
RN 405265-22-7 CAPLUS
CN 7,10-Methano-10H,16H-[1,4]dioxepino[5,6-b]diindolo[1,2,3-de:3',2',1'-ij]pyrrolo[3,4-g]quinoxaline-16,18(17H)-dione, 5a,7,8,10a-tetrahydro-19-methoxy-2-nitro-, (5aR,7R,10R,10aS,19S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L53 ANSWER 5 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
(Reactant or reagent)
(syntheses and antiproliferative activities of rebeccamycin derivs. with the sugar unit linked to both indole nitrogens)

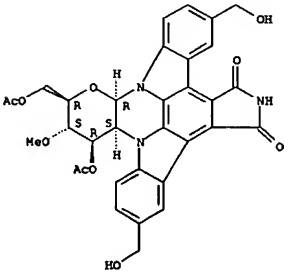
RN 340162-42-7 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-2,13-dicarboxaldehyde, 9-(acetyloxy)-7-[(acetyloxy)methyl]-5a,8,9,9a,16,17-hexahydro-8-methoxy-15,17-dioxo-, (5aR,7R,8S,9R,9aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 340162-44-9 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 9-(acetyloxy)-7-[(acetyloxy)methyl]-5a,8,9,9a-tetrahydro-2,13-bis(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

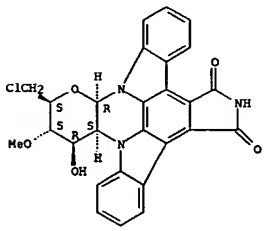
Absolute stereochemistry.



L53 ANSWER 5 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

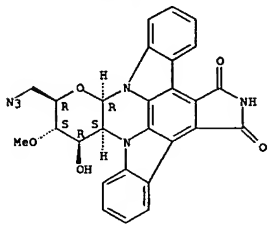
RN 340162-46-1 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 7-(chloromethyl)-5a,8,9,9a-tetrahydro-9-hydroxy-8-methoxy-, (5aR,7S,8S,9R,9aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



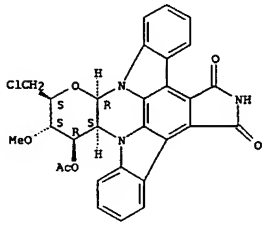
RN 340162-48-3 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 7-(azidomethyl)-5a,8,9,9a-tetrahydro-9-hydroxy-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



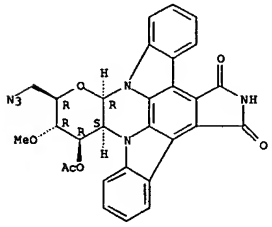
RN 340162-66-5 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 9-(acetyloxy)-7-[(acetyloxy)methyl]-5a,8,9,9a-tetrahydro-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX

L53 ANSWER 5 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 405265-20-5 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 9-(acetyloxy)-7-(azidomethyl)-5a,8,9,9a-tetrahydro-8-methoxy-, (5aR,7R,8R,9R,9aS)- (9CI) (CA INDEX NAME)

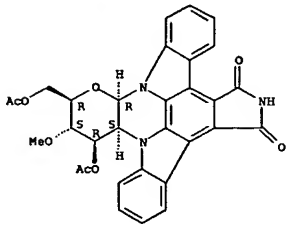
Absolute stereochemistry.



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

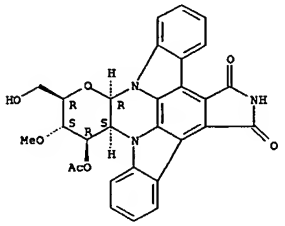
L53 ANSWER 5 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
NAME)

Absolute stereochemistry.



RN 340162-67-6 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 9-(acetyloxy)-5a,8,9,9a-tetrahydro-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 340162-68-7 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 9-(acetyloxy)-7-(chloromethyl)-5a,8,9,9a-tetrahydro-8-methoxy-, (5aR,7S,8S,9R,9aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L53 ANSWER 6 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:453056 CAPLUS
DOCUMENT NUMBER: 135:61238
TITLE: Preparation of maleimide and carbazole derivatives for the treatment of proliferative diseases
INVENTOR(S): Al-Awar, Rima Salim; Hecker, Kyle Andrew; Huang, Jianping; Joseph, Sajan; Ray, James Edward; Waid, Philip Parker
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001044235	A2	20010621	WO 2000-US33274	20001218
WO 2001044235	A3	20020117		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1250334	A2	20021023	EP 2000-989233	20001218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003092676	A1	20030515	US 2002-130801	20020521

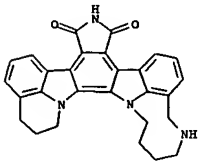
PRIORITY APPLN. INFO.: US 1999-171219P P 19991216
US 1999-171269P P 19991216
WO 2000-US33274 W 20001218
OTHER SOURCE(S): MARPAT 135:61238
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; A, B = O, S; X, Y = H; or X and Y, taken together, form a bond; R1 = H, alkyl; R5, R51 = halo, CN, alkyl, etc.; R6, R61 = alkyl; R7, R71 = alkoxycarbonyl, (CH2)mZ; Z = halo, OH, CO2H, etc.; Q1, Q6 = O, SOn, (CH2)1-3; Q2, Q5 = carbon-carbon single or double bond, NH, etc.; Q3, Q4 = (CH2)1-3; m = 0-5; n = 0-2], useful for inhibiting CDK4, were prepd. and formulated. E.g., a multi-step synthesis of II.HCl which showed activity (0.6051 .mu.M) in assay of cyclin D1-cdk4 kinase with the ING peptide as substrate, was given. Some of compds. I were found to inhibit cell growth and to inhibit Rb (retinoblastoma protein) phosphorylation.

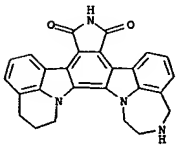
IT **345333-95-1P 345333-99-5P 345334-05-6P 345334-17-0P 345334-29-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of maleimide and carbazole derivs. for the treatment of

L53 ANSWER 6 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
proliferative diseases)
RN 345333-95-1 CAPLUS
CN 10H,16H-[1,5]Diazonino[3,2,1-jk]pyrido[1',2',3':1,7]indolo[2,3-a]pyrrolo[3,4-c]carbazole-10,12(11H)-dione, 1,2,3,4,5,6,17,18-octahydro-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

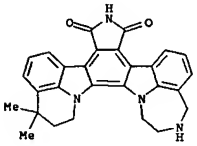
RN 345333-99-5 CAPLUS
CN 8H,14H-[1,4]Diazepino[6,7,1-jk]pyrido[1',2',3':1,7]indolo[2,3-a]pyrrolo[3,4-c]carbazole-8,10(9H)-dione, 1,2,3,4,15,16-hexahydro-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

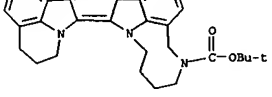
RN 345334-05-6 CAPLUS
CN 8H,14H-[1,4]Diazepino[6,7,1-jk]pyrido[1',2',3':1,7]indolo[2,3-a]pyrrolo[3,4-c]carbazole-8,10(9H)-dione, 1,2,3,4,15,16-hexahydro-15,15-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)

L53 ANSWER 6 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

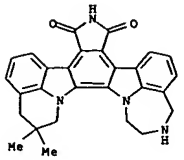


● HCl

IT 345336-85-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of maleimide and carbazole derivs. for the treatment of proliferative diseases)
RN 345336-85-8 CAPLUS
CN 10H,16H-[1,5]Diazonino[3,2,1-jk]pyrido[1',2',3':1,7]indolo[2,3-a]pyrrolo[3,4-c]carbazole-5(6H)-carboxylic acid, 1,2,3,4,11,12,17,18-octahydro-10,12-dioxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

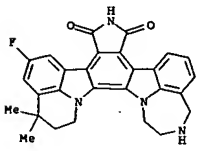


L53 ANSWER 6 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



● HCl

RN 345334-17-0 CAPLUS
CN 8H,14H-[1,4]Diazepino[6,7,1-jk]pyrido[1',2',3':1,7]indolo[2,3-a]pyrrolo[3,4-c]carbazole-8,10(9H)-dione, 12-fluoro-1,2,3,4,15,16-hexahydro-14,14-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 345334-29-4 CAPLUS
CN 8H,14H-[1,4]Diazepino[6,7,1-jk]pyrido[1',2',3':1,7]indolo[2,3-a]pyrrolo[3,4-c]carbazole-8,10(9H)-dione, 1,2,3,4,15,16-hexahydro-14,14-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)

L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:372160 CAPLUS
DOCUMENT NUMBER: 134:366738
TITLE: Preparation of 12,13-(pyranosyl)indolo[2,3-a]pyrrolo[3,4-c]carbazole and 12,13-(pyranosyl)furo[3,4-c]indolo[2,3-a]carbazole compounds as antitumor agents and method for their preparation
INVENTOR(S): Prudhomme, Michelle; Moreau, Pascale; Anizon, Fabrice; Marminon, Christelle; Atassi, Ghanem; Pierre, Alanin; Pfeiffer, Bruno; Renard, Pierre
PATENT ASSIGNEE(S): Adir Et Compagnie, Fr.
SOURCE: Jpn. Kokai Tokkyo Koho, 21 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001139578	A2	20010522	JP 2000-346837	20001114
FR 2801054	A1	20010518	FR 1999-14433	19991117
FR 2801054	B1	20030613		
EP 1101770	A1	20010523	EP 2000-403107	20001109
EP 1101770	B1	20030416		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 237625	E	20030515	AT 2000-403107	20001109
NO 2000005796	A	20010518	NO 2000-5796	20001116
NZ 508231	A	20010928	NZ 2000-508231	20001116
ZA 2000006729	A	20010605	ZA 2000-6729	20001117
BR 2000005426	A	20010703	BR 2000-5426	20001117
CN 1303859	A	20010718	CN 2000-128541	20001117
US 2002055510	A1	20020509	US 2001-10379	20011105
US 6569858	B2	20030527		

PRIORITY APPLN. INFO.: FR 1999-14433 A 19991117
US 2000-714746 A1 20001116
OTHER SOURCE(S): MARPAT 134:366738
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

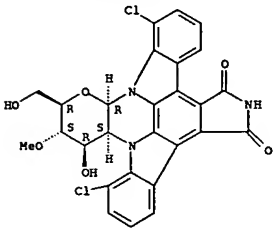
AB The title compds. [I; R1, R2 = U-V; U = single bond, linear or branched alkyl C1-6 alkylene optionally substituted by 1.gtoreq. substituents and/or 1.gtoreq. unsatd. bonds; V = H, halo, cyano, NO2, N3, linear or branched C1-6 alkyl, aryl, aryl-linear or branched C1-6 alkyl, HO, linear or branched C1-6 alkoxy, aryloxy, aryl-linear or branched C1-6 alkoxy, CHO, CO2H, (un)substituted carbamoyl, NH2, etc.; R4, R5 = H, halo, HO, linear or branched C1-6 alkoxy or alkyl, aryloxy, aryl-linear or branched C1-6 alkoxy, aryl, (un)substituted NH2, N3, (un)substituted N:NH, (un)substituted linear or branched alkyl C1-6 alkyl-carbonyloxy, aryl, aryl-linear or branched C1-6 alkyl, cycloalkyl, heterocycloalkyl; R6 = R4, CH2R4 (R4 = same as above); or an adjacent or nonadjacent pair of R4, R5, or R6 together with a carbon atom to which they are attached form a 3-6-membered ring contg. 1 or 2 O atoms; X, X1 = H, HO, linear or branched C1-6 alkoxy or alkylthio, SH; Y, Y1 = H or X and Y or X1 and Y1 together with the carbon atom to which they are bonded represent CO; G = O,

L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
(un)substituted NH] or pharmacol. acceptable salts thereof are prepd. These compds. possess in vitro and in vivo cytotoxicity and effect on cell cycle and are useful as antitumor agents (no data). Thus, 1 equiv K2CO3 and 1 equiv tosyl chloride were added to a soln. of 1.7 mmol rebeccamycin in 200 mL THF and refluxed fro 48 h to give 1,11-dichloro-12-(4-O-methyl-2-O-tosyl-.beta.-D-glucopyranosyl)-6,7,12,13-tetrahydro-(5H)-indolo[2,3-a]pyrrolo[3,4-c]carbazole-5,7-dione which was heated with 10 equiv NaN3 in DMF at 70.degree. for 6 h, followed by hydrolysis and extn. with EtOAc to give 1,11-dichloro-12,13-(1,2-(4-O-methyl-.beta.-D-mannopyranosyl))-6,7,12,13-tetrahydro-(5H)-indolo[2,3-a]pyrrolo[3,4-c]carbazole-5,7-dione (II).

IT 340162-37-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of (pyranosyl)indolo[2,3-a]pyrrolo[c]carbazole and (pyranosyl)furo[c]indolo[a]carbazole compds. as antitumor agents and method for prepn.)

RN 340162-37-0 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 4,11-dichloro-5a,8,9,9a-tetrahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

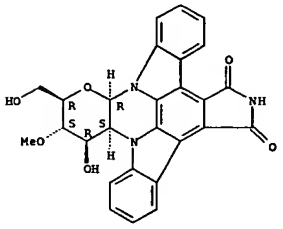


IT 340162-38-1P 340162-40-5P 340162-41-6P
340162-42-7P 340162-43-8P 340162-44-9P
340162-45-0P 340162-46-1P 340162-47-2P
340162-48-3P 340162-49-4P 340162-50-7P
340162-51-8P 340162-52-9P 340162-53-0P
340162-54-1P 340162-55-2P 340162-56-3P
340162-57-4P 340162-58-5P 340162-59-6P
340162-60-9P 340162-61-0P 340162-62-1P
340162-63-2P 340162-64-3P 340162-65-4P
340162-66-5P 340162-67-6P 340162-68-7P

L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
340162-69-8P 340162-70-1P 340162-71-2P
340162-72-3P 340162-73-4P 340162-74-5P
340162-75-6P 340162-76-7P 340162-77-8P
340162-78-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of (pyranosyl)indolo[2,3-a]pyrrolo[c]carbazole and (pyranosyl)furo[c]indolo[a]carbazole compds. as antitumor agents and method for prepn.)

RN 340162-38-1 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 5a,8,9,9a-tetrahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

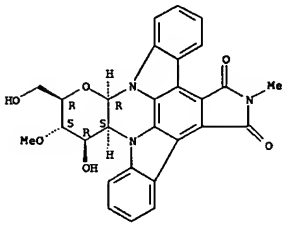
Absolute stereochemistry.



RN 340162-40-5 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 5a,8,9,9a-tetrahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-16-methyl-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

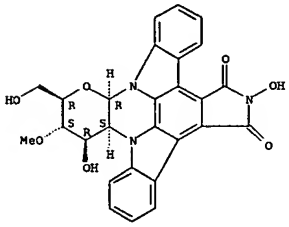
Absolute stereochemistry.

L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 340162-41-6 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 5a,8,9,9a-tetrahydro-9,16-dihydroxy-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

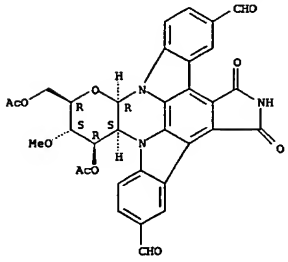
Absolute stereochemistry.



RN 340162-42-7 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-2,13-dicarboxaldehyde, 9-(acetyloxy)-7-[(acetyloxy)methyl]-5a,8,9,9a,16,17-hexahydro-8-methoxy-15,17-dioxo-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

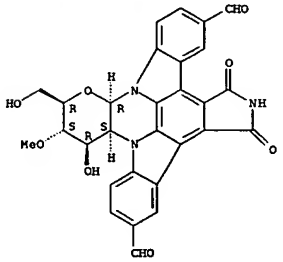
Absolute stereochemistry.

L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 340162-43-8 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-2,13-dicarboxaldehyde, 5a,8,9,9a,16,17-hexahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-15,17-dioxo-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

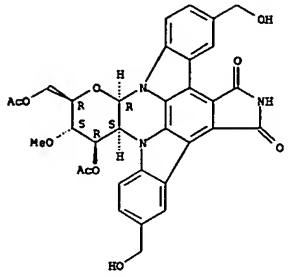
Absolute stereochemistry.



RN 340162-44-9 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 9-(acetyloxy)-7-[(acetyloxy)methyl]-5a,8,9,9a-tetrahydro-2,13-bis(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

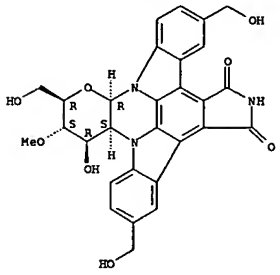
Absolute stereochemistry.

L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 340162-45-0 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 5a,8,9,9a-tetrahydro-9-hydroxy-2,7,13-tris(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 340162-46-1 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 7-(chloromethyl)-5a,8,9,9a-tetrahydro-9-hydroxy-8-methoxy-, (5aR,7S,8S,9R,9aS)- (9CI) (CA INDEX NAME)

L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

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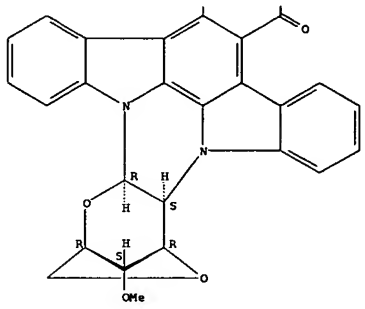
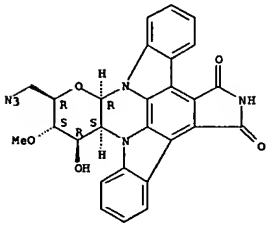


RN 340162-48-3 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 7-(azidomethyl)-5a,8,9,9a-tetrahydro-9-hydroxy-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

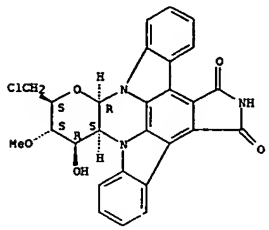
Absolute stereochemistry.



RN 340162-49-4 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 5a,8,9,9a-tetrahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-2,13-dinitro-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
Absolute stereochemistry.



RN 340162-47-2 CAPLUS
CN 7,10-Methano-10H,16H-[1,4]dioxepino[5,6-b]diindolo[1,2,3-de:3',2',1'-ij]pyrrolo[3,4-g]quinoxaline-16,18(17H)-dione, 5a,7,8,10a-tetrahydro-19-methoxy-, (5aR,7R,10R,10aS,19S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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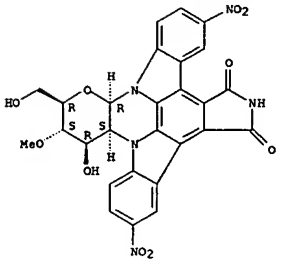
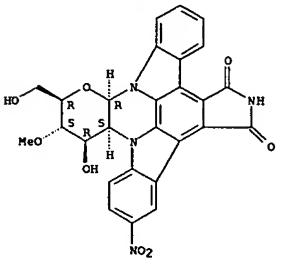
L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 340162-50-7 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 5a,8,9,9a-tetrahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-13-nitro-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

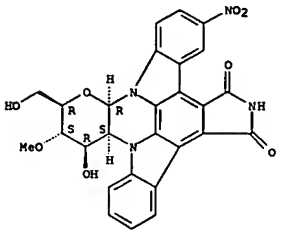
Absolute stereochemistry.



RN 340162-51-8 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 5a,8,9,9a-tetrahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-2-nitro-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

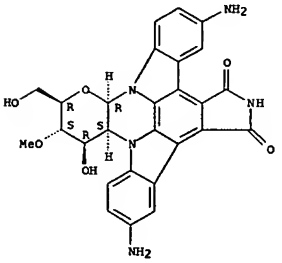
Absolute stereochemistry.

L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 340162-52-9 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 2,13-diamino-5a,8,9,9a-tetrahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 340162-53-0 CAPLUS
CN 7,10-Methano-10H,16H-[1,4]dioxepino[5,6-b]diindolo[1,2,3-de:3',2',1'-ij]pyrrolo[3,4-g]quinoxaline-16,18(17H)-dione, 5a,7,8,10a-tetrahydro-19-methoxy-2,14-dinitro-, (5aR,7R,10R,10aS,19S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

CN 7,10-Methano-10H,16H-[1,4]dioxepino[5,6-b]diindolo[1,2,3-de:3',2',1'-ij]pyrrolo[3,4-g]quinoxaline-16,18(17H)-dione, 5a,7,8,10a-tetrahydro-19-methoxy-14-nitro-, (5aR,7R,10R,10aS,19S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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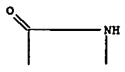

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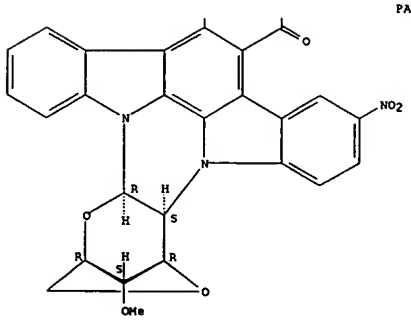

L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

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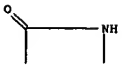

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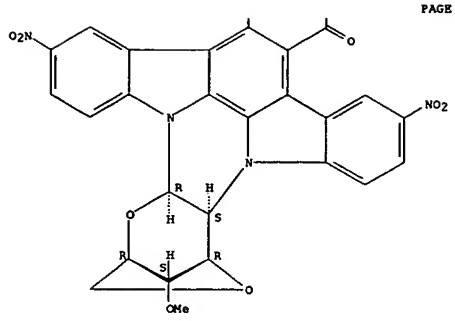
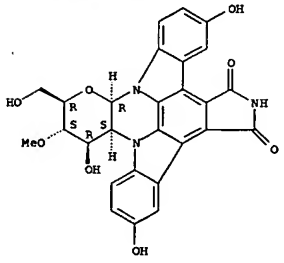


RN 340162-54-1 CAPLUS

L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

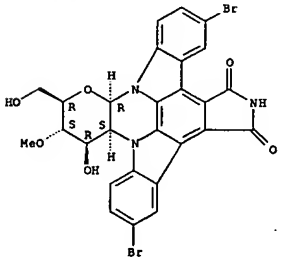
RN 340162-55-2 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 5a,8,9,9a-tetrahydro-2,9,13-trihydroxy-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 340162-56-3 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 2,13-dibromo-5a,8,9,9a-tetrahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

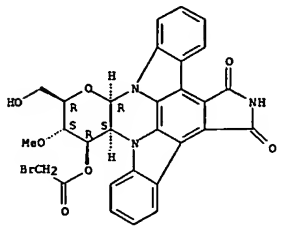
Absolute stereochemistry.



RN 340162-57-4 CAPLUS
CN Acetic acid, bromo-, (5aR,7R,8S,9R,9aS)-5a,8,9,9a,16,17-hexahydro-7-(hydroxymethyl)-8-methoxy-15,17-dioxo-7H,15H-diindolo[1,2,3-de:3',2',1'-

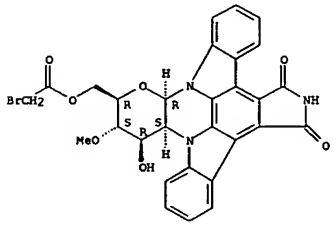
L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxalin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 340162-58-5 CAPLUS
CN Acetic acid, bromo-, [(5aR,7R,8S,9R,9aS)-5a,8,9,9a,16,17-hexahydro-9-hydroxy-8-methoxy-15,17-dioxo-7H,15H-diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxalin-7-yl]methyl ester (9CI) (CA INDEX NAME)

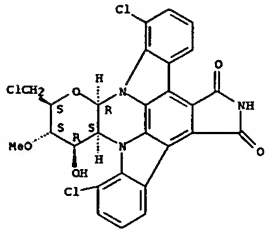
Absolute stereochemistry.



RN 340162-59-6 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 4,11-dichloro-7-(chloromethyl)-5a,8,9,9a-tetrahydro-9-hydroxy-8-methoxy-, (5aR,7S,8S,9R,9aS)- (9CI) (CA INDEX NAME)

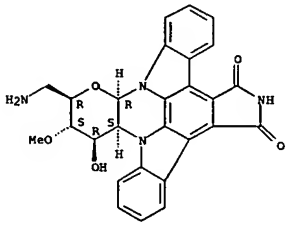
Absolute stereochemistry.

L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 340162-60-9 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 7-(aminomethyl)-5a,8,9,9a-tetrahydro-9-hydroxy-8-methoxy-, monohydrochloride, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

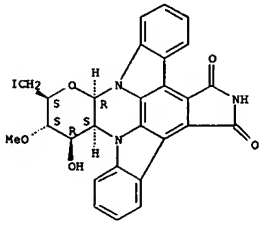


● HCl

RN 340162-61-0 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 5a,8,9,9a-tetrahydro-9-hydroxy-7-(iodomethyl)-8-methoxy-, (5aR,7S,8S,9R,9aS)- (9CI) (CA INDEX NAME)

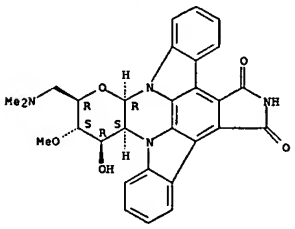
Absolute stereochemistry.

L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 340162-62-1 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 7-[(dimethylamino)methyl]-5a,8,9,9a-tetrahydro-9-hydroxy-8-methoxy-, monohydrochloride, (5aR,7R,8S,9R,9aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

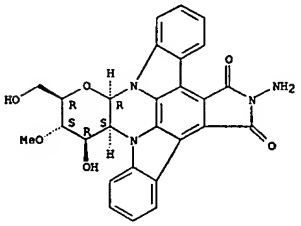


● HCl

RN 340162-63-2 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 16-amino-5a,8,9,9a-tetrahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

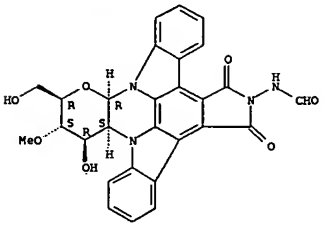
Absolute stereochemistry.

L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 340162-64-3 CAPLUS
CN Formamide, N-[(5aR,7R,8S,9R,9aS)-5a,8,9,9a,15,17-hexahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-15,17-dioxo-7H,16H-diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxalin-16-yl]- (9CI) (CA INDEX NAME)

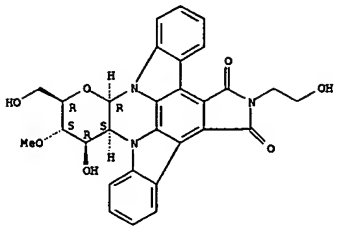
Absolute stereochemistry.



RN 340162-65-4 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 5a,8,9,9a-tetrahydro-9-hydroxy-16-(2-hydroxyethyl)-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

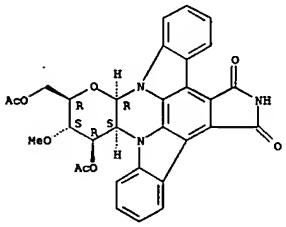
Absolute stereochemistry.

L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 340162-66-5 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 9-(acetyloxy)-7-[(acetyloxy)methyl]-5a,8,9,9a-tetrahydro-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

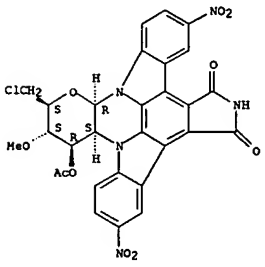
Absolute stereochemistry.



RN 340162-67-6 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 9-(acetyloxy)-5a,8,9,9a-tetrahydro-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

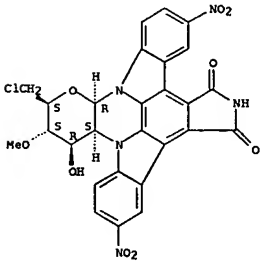
Absolute stereochemistry.

L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 340162-70-1 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 7-(chloromethyl)-5a,8,9,9a-tetrahydro-9-hydroxy-8-methoxy-2,13-dinitro-, (5aR,7S,8S,9R,9aS)- (9CI) (CA INDEX NAME)

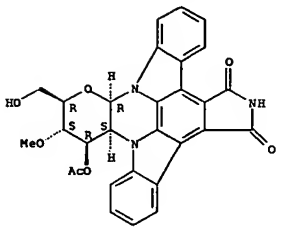
Absolute stereochemistry.



RN 340162-71-2 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 7-(azidomethyl)-5a,8,9,9a-tetrahydro-9-hydroxy-8-methoxy-2,13-dinitro-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

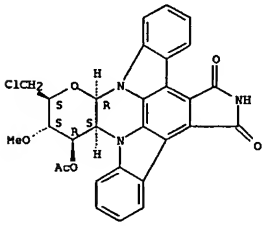
Absolute stereochemistry.

L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 340162-68-7 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 9-(acetyloxy)-7-(chloromethyl)-5a,8,9,9a-tetrahydro-8-methoxy-, (5aR,7S,8S,9R,9aS)- (9CI) (CA INDEX NAME)

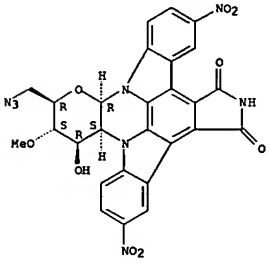
Absolute stereochemistry.



RN 340162-69-8 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 9-(acetyloxy)-7-(chloromethyl)-5a,8,9,9a-tetrahydro-8-methoxy-2,13-dinitro-, (5aR,7S,8S,9R,9aS)- (9CI) (CA INDEX NAME)

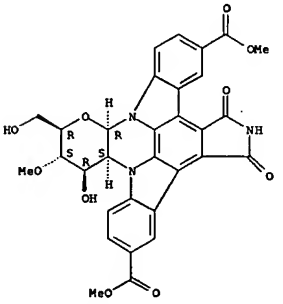
Absolute stereochemistry.

L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 340162-72-3 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-2,13-dicarboxylic acid, 5a,8,9,9a,16,17-hexahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-15,17-dioxo-, dimethyl ester, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

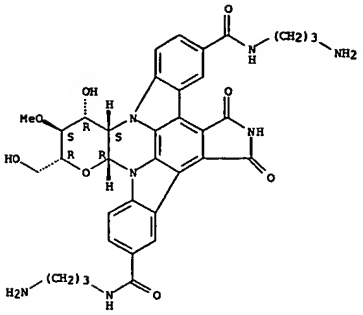
Absolute stereochemistry.



RN 340162-73-4 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-2,13-dicarboxamide, N,N'-bis(3-aminopropyl)-5a,8,9,9a,16,17-hexahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-15,17-dioxo-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

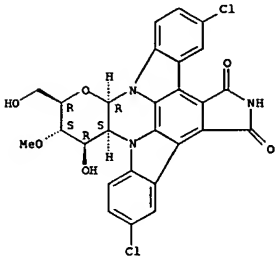
Absolute stereochemistry.

L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 340162-74-5 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 2,13-dichloro-5a,8,9,9a-tetrahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

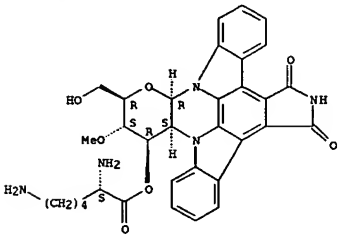
Absolute stereochemistry.



L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

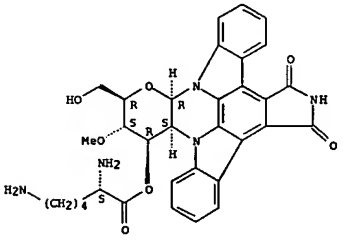
RN 340162-77-8 CAPLUS
CN L-Lysine, (5aR,7R,8S,9R,9aS)-5a,8,9,9a,16,17-hexahydro-7-(hydroxymethyl)-8-methoxy-15,17-dioxo-7H,15H-diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxalin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 340162-78-9 CAPLUS
CN L-Lysine, (5aR,7R,8S,9R,9aS)-5a,8,9,9a,16,17-hexahydro-7-(hydroxymethyl)-8-methoxy-15,17-dioxo-7H,15H-diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxalin-9-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

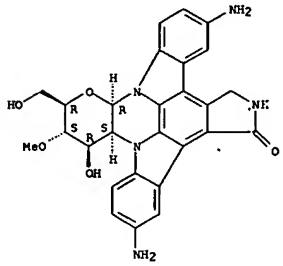
Absolute stereochemistry.



● HCl

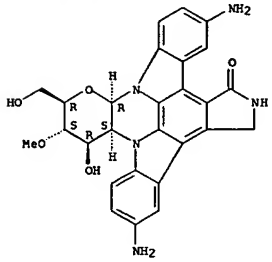
L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
RN 340162-75-6 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxalin-15-one, 2,13-diamino-5a,8,9,9a,16,17-hexahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 340162-76-7 CAPLUS
CN 7H,17H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxalin-17-one, 2,13-diamino-5a,8,9,9a,15,16-hexahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L53 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

L53 ANSWER 8 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:319711 CAPLUS
DOCUMENT NUMBER: 134:331632
TITLE: Pharmaceutical compositions containing protein kinase C inhibitors and antioxidants
INVENTOR(S): Cameron, Norman Eugene; Ways, Douglas Kirk
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

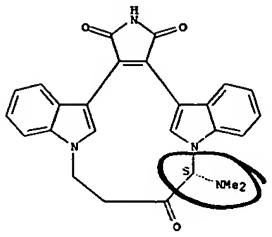
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001030331	A2	20010503	WO 2000-US26254	20001013
WO 2001030331	A3	20020124		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-161129P P 19991022
US 2000-177510P P 20000121
OTHER SOURCE(S): MARPAT 134:331632
AB Compns. comprising a PKC inhibitor, or a salt and an antioxidant, essential fatty acid, or a prostacyclin agent, or a pharmaceutically acceptable salt thereof are provided. Also provided are methods of treatment comprising administration of such compns., and methods of treatment comprising co-administration of a PKC inhibitor, or a pharmaceutically acceptable salt thereof, and an antioxidant, essential fatty acid, or a prostacyclin agent, or a salt. Thus, an aerosol contained drug 0.35, EtOH 29.75, propellant-22 70.0%.
IT 336609-86-0D, derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. contg. protein kinase C inhibitors and antioxidants)
RN 336609-86-0 CAPLUS
CN 5,19:10,15-Dimetheno-16H-dibenzo[g,m]pyrrolo[3,4-j][1,6]diazacyclotetradecine-7,16,18(6H,17H)-trione, 6-(dimethylamino)-8,9-dihydro-, (6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L53 ANSWER 8 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

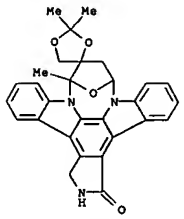


L53 ANSWER 9 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:178436 CAPLUS
DOCUMENT NUMBER: 134:227381
TITLE: Particle-forming compositions containing fused pyrrolocarbazoles
INVENTOR(S): Dickason, David A.; Patel, Piyush R.; Corvari, Vincent; Shek, Efraim; Herman, Joseph L.; Skell, Jeffry M.
PATENT ASSIGNEE(S): Cephalon, Inc., USA
SOURCE: U.S., 18 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6200968	B1	20010313	US 1999-368409	19990805
CA 2338546	AA	20000217	CA 1999-2338546	19990806
EP 1102758	A1	20010530	EP 1999-940914	19990806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003524597	T2	20030819	JP 2000-563637	19990806

PRIORITY APPLN. INFO.: US 1998-95611P P 19980806
US 1999-368409 A 19990805
WO 1999-US17795 W 19990806
OTHER SOURCE(S): MARPAT 134:227381
AB A non-aq., particle-forming compn. contg. fused pyrrolocarbazole and a surfactant is disclosed. Upon contact with an aq. medium, the particle-forming compn. spontaneously disperses into suspended particles, thereby forming a stable suspension that provides greatly improved bioavailability of orally administered fused pyrrolocarbazole compds. Pyrrolocarbazoles-contg. compns. are useful for treatment of neurol. disorders and cancer, esp. prostate cancer, in mammals.
IT 329684-24-4
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(prepn. and therapeutic use of particle-forming compns. contg. fused pyrrolocarbazoles with improved bioavailability)
RN 329684-24-4 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2',3',11',12'-tetrahydro-2,2,9'-trimethyl- (9CI) (CA INDEX NAME)

L53 ANSWER 9 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 10 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:20587 CAPLUS
DOCUMENT NUMBER: 134:160791
TITLE: Protein kinase C .beta.I is implicated in the regulation of neuroblastoma cell growth and proliferation
AUTHOR(S): Svensson, Karin; Zeidman, Ruth; Troller, Ulrika; Schultz, Anna; Larsson, Christer
CORPORATE SOURCE: Department of Laboratory Medicine, Molecular Medicine, Malmo University Hospital, Lund University, Malmo, 205 02, Swed.
SOURCE: Cell Growth & Differentiation (2000), 11(12), 641-648
CODEN: CGDIE7; ISSN: 1044-9523
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

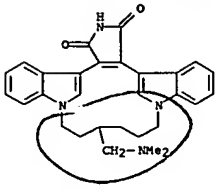
AB To investigate a putative involvement of protein kinase C (PKC) isoforms in supporting neuroblastoma cell proliferation, SK-N-BE(2) neuroblastoma cells were transfected with expression vectors coding for the C2 and V5 regions from different PKC isoforms. These structures have been suggested to inhibit the activity of their corresponding PKC isoform. The PKC fragments were fused to enhanced green fluorescent protein to facilitate the detection of transfected cells. Expression of the C2 domain from a classical PKC isoform (PKC.alpha.), but not of C2 domains from novel PKC.delta. or PKC.epsilon., suppressed the no. of neuroblastoma cells pos. for cyclin A and bromodeoxyuridine incorporation. This indicates a role for a classical isoform in regulating proliferation of these cells. Among the V5 fragments from PKC.alpha., PKC.beta.I, and PKC.beta.II, the PKC.beta.I V5 had the most suppressive effect on proliferation markers, and this fragment also displaced PKC.beta.I from the nucleus. Furthermore, a PKC.beta.-specific inhibitor, LY379196, suppressed the phorbol ester- and serum-supported growth of neuroblastoma cells. There was a marked enhancement by LY379196 of the growth-suppressive and/or cytotoxic effects of paclitaxel and vincristine. These results indicate that PKC.beta.I has a pos. effect on the growth and proliferation of neuroblastoma cells and demonstrate that inhibition of PKC.beta. may be used to enhance the effect of microtubule-interacting anticancer agents on neuroblastoma cells.

IT 259754-09-1, LY 379196
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(protein kinase C .beta. inhibitor; LY 379196; protein kinase C .beta.I in regulation of neuroblastoma cell growth and proliferation in relation to)

RN 259754-09-1 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-[(dimethylamino)methyl]-6,7,8,9,10,11-hexahydro-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 259754-08-0
CMF C29 H30 N4 O2



CM 2

CRN 75-75-2
CMF C H4 O3 S

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

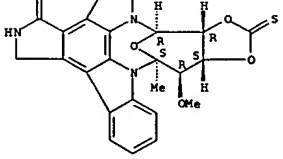
L53 ANSWER 11 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:291484 CAPLUS
DOCUMENT NUMBER: 133:89714
TITLE: Synthesis and antiangiogenic activity of staurosporine derivatives
AUTHOR(S): Li, Zhuorong; Sunazuka, Toshiaki; Yamada, Rintaro; Kato, Yumiko; Enomoto, Akiko; Hayashi, Masahiko; Harigaya, Yoshihiro; Omura, Satoshi
CORPORATE SOURCE: Research Center for Biological Function, The Kitasato Institute, and Kitasato University, Minato-ku, Tokyo, 108, Japan
SOURCE: Journal of Antibiotics (2000), 53(4), 426-429
CODEN: JANTAJ; ISSN: 0021-8820
PUBLISHER: Japan Antibiotics Research Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The synthesis and antiangiogenic activity of staurosporine derivs. with modified amino sugar moieties is reported. Some of the compds. prepd. showed decreased antiangiogenic activity, but significantly decreased cytotoxicity and prominent selective toxicity. The most promising compd. also inhibited the tumor angiogenesis caused by tumor inoculation in mice in vivo.

IT 282103-06-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and antiangiogenic activity of staurosporine derivs.)

RN 282103-06-4 CAPLUS
CN 6,11-Epoxy-6H,19H-[1,3]dioxolo[4,5-c]diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonin-19-one, 6a,9a,10,11,17,18-hexahydro-10-methoxy-11-methyl-8-thioxo-, (6R,6aR,9aS,10R,11S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

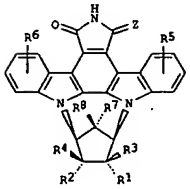


REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

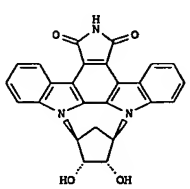
L53 ANSWER 12 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:31347 CAPLUS
DOCUMENT NUMBER: 132:78734
TITLE: Preparation of indolocarbazole derivatives useful for the treatment of neurodegenerative diseases characterized by tau hyperphosphorylation and cancer
INVENTOR(S): Roder, Hanno; Lowinger, Timothy B.; Brittelli, David R.; Vanzandt, Michael C.
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: U.S., 23 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6013646	A	20000111	US 1998-109131	19980702
CA 2336419	AA	20000113	CA 1999-2336419	19990623
WO 2000001699	A1	20000113	WO 1999-EP4369	19990623
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9947766	A1	20000124	AU 1999-47766	19990623
AU 754399	B2	20021114		
EP 1091962	A1	20010418	EP 1999-931158	19990623
R: DE, ES, FR, GB, IT				
JP 2002519425	T2	20020702	JP 2000-558102	19990623
US 6541468	B1	20030401	US 1999-382539	19990825

PRIORITY APPLN. INFO.: US 1998-109131 A 19980702
WO 1999-EP4369 W 19990623
OTHER SOURCE(S): MARPAT 132:78734
GI



I



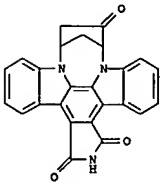
II

AB Indolocarbazoles I [R1 = H, OH, carboxy, carboxamido, alkyloxyalkyl; R2, R3, R4 = H, OH; R5, R6 = H, OH, amino, acylamino, acyloxy, alkyloxy,

L53 ANSWER 12 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
carboxy, carboxamido, halogen; R7, R8 = H, OH, halogen; R7R8 = oxo; Z = O, H2], which are analogs of K 252a, a naturally occurring alkaloid, were prepd. for potential use in the treatment of neurodegenerative diseases characterized by tau hyperphosphorylation, such as Alzheimer's disease (AD), frontal lobe degeneration (FLD), argyrophilic grains disease, subacute sclerotizing panencephalitis (SSPE), and cancer. Thus, indolocarbazole II was prepd. in a 5 step synthetic sequence starting from (1R,3S)-4-cyclopentene-1,3-diol monoacetate and 12,13-dihydro-6-[(4-methoxyphenyl)methyl]-5H-indolo[2,3-a]pyrrolo[3,4-c]carbazole-5,7(6H)-dione. The prepd. compds. were assayed for cAMP-dependent kinase and cdc2 kinase inhibiting activity.

IT **233253-35-5P 233253-37-7P 253680-44-3P**
253680-48-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of indolocarbazole derivs. useful for the treatment of neurodegenerative diseases characterized by tau hyperphosphorylation and cancer)

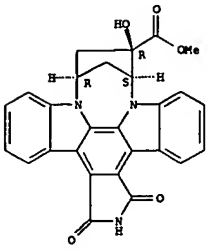
RN 233253-35-5 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-1,3,10(2H,9H)-trione, 11,12-dihydro- (9CI) (CA INDEX NAME)



RN 233253-37-7 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10-carboxylic acid, 2,3,9,10,11,12-hexahydro-10-hydroxy-1,3-dioxo-, methyl ester, (9R,10S,12S)-rel- (9CI) (CA INDEX NAME)

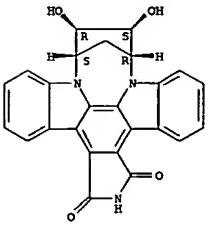
Relative stereochemistry.

L53 ANSWER 12 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 253680-44-3 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-1,3(2H)-dione, 9,10,11,12-tetrahydro-10,11-dihydroxy-, (9R,10S,11R,12S)-rel- (9CI) (CA INDEX NAME)

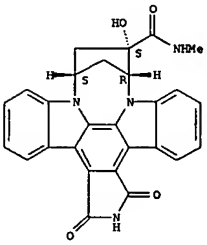
Relative stereochemistry.



RN 253680-48-7 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10-carboxamide, 2,3,9,10,11,12-hexahydro-10-hydroxy-N-methyl-1,3-dioxo-, (9R,10S,12S)-rel- (9CI) (CA INDEX NAME)

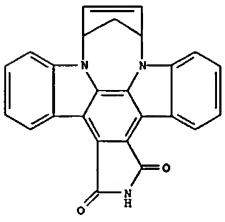
Relative stereochemistry.

L53 ANSWER 12 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



IT **233253-33-3P 253680-52-3P 253680-57-8P**
253680-58-9P 253680-60-3P 253680-62-5P
253680-64-7P 253680-66-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of indolocarbazole derivs. useful for the treatment of neurodegenerative diseases characterized by tau hyperphosphorylation and cancer)

RN 233253-33-3 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-1,3(2H)-dione, 9,12-dihydro- (9CI) (CA INDEX NAME)



RN 253680-52-3 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-1,3(2H)-dione, 9,12-dihydro-2-[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

L53 ANSWER 12 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

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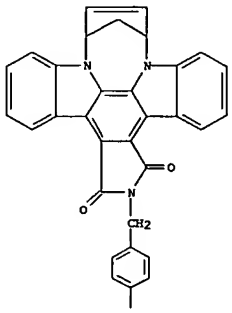

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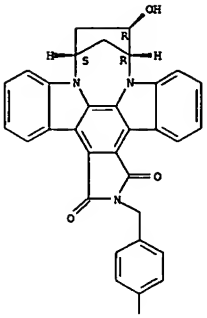
RN 253680-57-8 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-1,3(2H)-dione, 9,10,11,12-tetrahydro-10-hydroxy-2-[(4-methoxyphenyl)methyl]-, (9R,10R,12S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L53 ANSWER 12 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

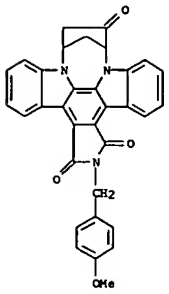
PAGE 1-A



PAGE 2-A

RN 253680-58-9 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-1,3,10(2H,9H)-trione, 11,12-dihydro-2-[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

L53 ANSWER 12 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

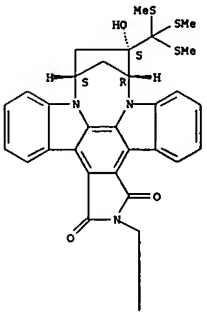


RN 253680-60-3 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-1,3(2H)-dione, 9,10,11,12-tetrahydro-10-hydroxy-2-[(4-methoxyphenyl)methyl]-10-[tris(methylthio)methyl]-, (9R,10S,12S)-rel- (9CI) (CA INDEX NAME)

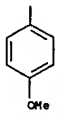
Relative stereochemistry.

L53 ANSWER 12 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

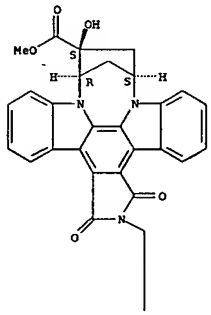


RN 253680-62-5 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10-carboxylic acid, 2,3,9,10,11,12-hexahydro-10-hydroxy-2-[(4-methoxyphenyl)methyl]-1,3-dioxo-, methyl ester, (9R,10S,12S)-rel- (9CI) (CA INDEX NAME)

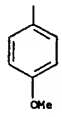
Relative stereochemistry.

L53 ANSWER 12 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



RN 253680-64-7 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10-carboxylic acid, 2,3,9,10,11,12-hexahydro-10-hydroxy-2-[(4-methoxyphenyl)methyl]-1,3-dioxo-, (9R,10S,12S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L53 ANSWER 12 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

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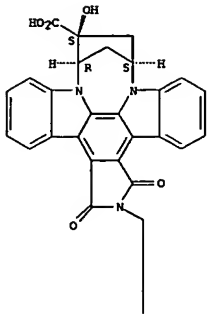
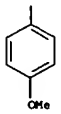


PAGE 2-A



RN 253680-66-9 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10-carboxamide, 2,3,9,10,11,12-hexahydro-10-hydroxy-2-[(4-methoxyphenyl)methyl]-N-methyl-1,3-dioxo-, (9R,10S,12S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L53 ANSWER 12 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

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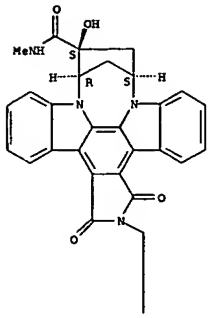
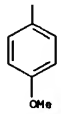


PAGE 2-A



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 13 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:8352 CAPLUS
DOCUMENT NUMBER: 132:192147
TITLE: Effects of protein kinase C inhibitors on thromboxane production by thrombin-stimulated platelets
AUTHOR(S): Samokhin, G. P.; Jirousek, M. R.; Ways, D. K.; Henriksen, R. A.
CORPORATE SOURCE: Endocrine Research, Lilly Research Laboratories, Indianapolis, IN, USA
SOURCE: European Journal of Pharmacology (1999), 386(2/3), 297-303
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The purpose of these studies was to identify a possible role for protein kinase C in thromboxane prodn. The effects of four putative protein kinase C inhibitors were studied with platelet stimulation by thrombin (0.5-150 nM), Thrombin Quick I (1.5-500 nM) or a thrombin receptor (protease activated receptor-1) agonist peptide (TRAP) (5-120 .mu.M). Thromboxane prodn. was increased by the bisindolylmaleimide deriv., 2-[1-(3-dimethylaminopropyl)-1H-indol-3-yl]-3-(1H-indol-3-yl)-maleimide (GF 109203X), unchanged by the inhibitors 12-(2-cyanoethyl)-6,7,12,13-tetrahydro-13-methyl-5-oxo-5H-indolo(2,3-a)pyrrolo(3,4-c)-carbazole (Go 6976) and 5,21:12,17-dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-[(dimethylamino)methyl]-6,7,8,9,10,11-hexahydro-, monomethanesulfonate (379196), the latter of which is protein kinase C .beta.-selective, and decreased by 1-[6-[(3-acetyl-2,4,6-trihydroxy-5-methylphenyl)methyl]-5,7-dihydroxy-2,2-dimethyl-2H-1-benzopyran-8-yl]-3-phenyl-2-propen-1-one (rottlerin), an inhibitor selective for protein kinase C .delta.. These results indicate complex regulation of thromboxane synthesis in human platelets including a probable role for protein kinase C .delta.. The results taken together further suggest that GF 109203X may suppress neg. feedback resulting from an unidentified kinase and that the classical protein kinase C isoforms .alpha. and .beta. do not have a significant role in regulating thromboxane prodn. by platelets.

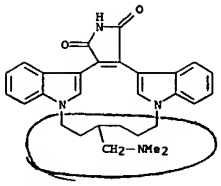
IT 259754-09-1, LY 379196
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(effects of protein kinase C inhibitors on thromboxane prodn. by thrombin-stimulated platelets)

RN 259754-09-1 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-[(dimethylamino)methyl]-6,7,8,9,10,11-hexahydro-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 259754-08-0
CMF C29 H30 N4 O2

L53 ANSWER 13 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



CM 2

CRN 75-75-2
CMF C H4 O3 S

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 14 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:701621 CAPLUS
DOCUMENT NUMBER: 132:35688
TITLE: Synthesis of indole-ring fluorine-labeled analogs of LY333531, an isoform-selective inhibitor of protein kinase C
AUTHOR(S): Goekjian, Peter G.; Lugo-Mas, Priscilla; Cable, Stacy L.; Cole, John O.; White, James W.; Thompson, Dale J.; Dudley, Tamara P.; Jirousek, Michael R.; Dixon, Jeffrey T.; Ballas, Lawrence M.
CORPORATE SOURCE: Department of Chemistry, Mississippi State University, Mississippi, MS, 39762, USA
SOURCE: Journal of Fluorine Chemistry (1999), 98(2), 137-142
CODEN: JFLCAR; ISSN: 0022-1139
PUBLISHER: Elsevier Science S.A.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:35688

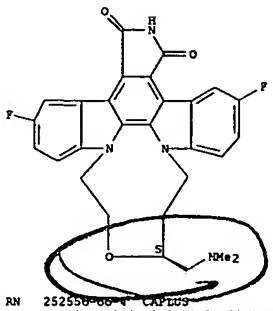
AB Two fluorine-labeled analogs of LY333531, a potent, ATP-competitive, and isoform-selective inhibitor of protein kinase C-beta, have been prepd. 19F-NMR labels were placed on the indole rings to probe for differences in the catalytic domains of the PKC isoforms. The fluorinated bis(indolyl)maleimide was prepd. by a Steglich coupling of 5-fluoroindole with N-methyldichloromaleimide, and was coupled to a chiral, aliph. dimesylate prepd. from 1(S)-[(2R)-1,4-dioxaspiro[4.5]decanyl]3-buten-1-ol. The coupling-macrocyclization step was performed by slow addn. of a mixt. of the bis(indolyl)maleimide and the dimesylate to a suspension of cesium carbonate in DMF, and adjustment of the functionality provided the final labeled analog. A simplified analog was prepd. from diiodohexane by a similar procedure. The analogs had IC(50)'s of 5 and 6 nM, resp., against PKC-beta(II), and of 57 and 79 nM, resp., against PKC-alpha.

IT **252556-65-3P 252556-66-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of indole-ring fluorine-labeled analogs of LY333531)

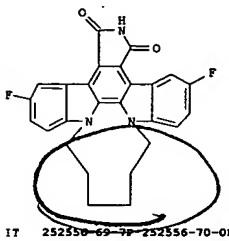
RN 252556-65-3 CAPLUS
CN 1H,12H-Diindolo[1,2,3-hi:3',2',1'-mn]pyrrolo[3,4-k][4,1,8]benzoxadiazecine-1,3(2H)-dione, 12-[(dimethylamino)methyl]-5,18-difluoro-9,10,13,14-tetrahydro-, (12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L53 ANSWER 14 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 252556-66-4 CAPLUS
CN 1H-Diindolo[1,2,3-hi:3',2',1'-mn]pyrrolo[3,4-k][1,8]benzodiazecine-1,3(2H)-dione, 5,18-difluoro-9,10,11,12,13,14-hexahydro- (9CI) (CA INDEX NAME)



IT **252556-69-7P 252556-70-0P 252556-71-1P**
252556-72-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of indole-ring fluorine-labeled analogs of LY333531)

RN 252556-69-7 CAPLUS
CN 1H,12H-Diindolo[1,2,3-hi:3',2',1'-mn]pyrrolo[3,4-k][4,1,8]benzoxadiazecine-1,3(2H)-dione, 12-(2R)-1,4-dioxaspiro[4.5]dec-2-yl-5,18-difluoro-9,10,13,14-tetrahydro-2-methyl-, (12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L53 ANSWER 14 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

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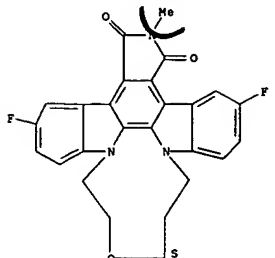

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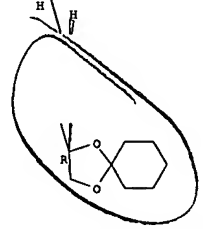
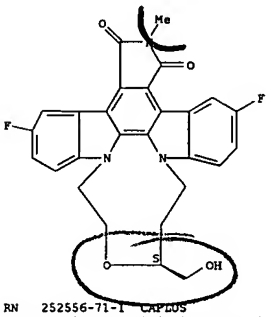


RN 252556-70-0 CAPLUS
CN 1H,12H-Diindolo[1,2,3-hi:3',2',1'-mn]pyrrolo[3,4-k][4,1,8]benzoxadiazecine-1,3(2H)-dione, 5,18-difluoro-9,10,13,14-tetrahydro-12-(hydroxymethyl)-2-methyl-, (12S)- (9CI) (CA INDEX NAME)

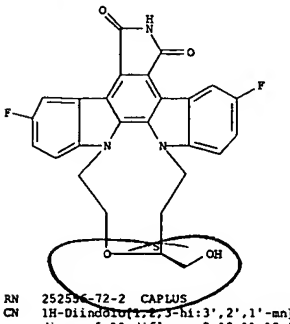
Absolute stereochemistry.

L53 ANSWER 14 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



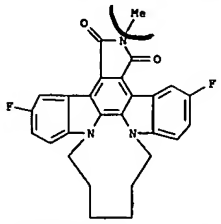
RN 252556-71-1 CAPLUS
CN 1H,12H-Diindolo[1,2,3-hi:3',2',1'-mn]pyrrolo[3,4-k][4,1,8]benzoxadiazecine-1,3(2H)-dione, 5,18-difluoro-9,10,13,14-tetrahydro-12-(hydroxymethyl)-, (12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 252556-72-2 CAPLUS
CN 1H-Diindolo[1,2,3-hi:3',2',1'-mn]pyrrolo[3,4-k][1,8]benzodiazecine-1,3(2H)-dione, 5,18-difluoro-9,10,11,12,13,14-hexahydro-2-methyl- (9CI) (CA INDEX NAME)

L53 ANSWER 14 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 15 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:460424 CAPLUS
DOCUMENT NUMBER: 131:87757
TITLE: Preparation of 3'-epimeric k-252a derivatives that enhance the function of cholinergic neurons
INVENTOR(S): Rudkins, Robert L.; Gingrich, Diane E.
PATENT ASSIGNEE(S): Cephalon, Inc., USA; Kyowa Hakko Kogyo Co., Ltd.
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9933836	A1	19990708	WO 1998-US27644	19981230
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2315953	AA	19990708	CA 1998-2315953	19981230
AU 9919474	A1	19990719	AU 1999-19474	19981230
US 6093713	A	20000725	US 1998-223518	19981230
BR 9814543	A	20001010	BR 1998-14543	19981230
EP 1044203	A1	20001018	EP 1998-964309	19981230
EP 1044203	B1	20030312		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2001527079	T2	20011225	JP 2000-526515	19981230
AT 234308	E	20030315	AT 1998-964309	19981230
US 6451786	B1	20020917	US 2000-503812	20000215
NO 2000003397	A	20000831	NO 2000-3397	20000629

PRIORITY APPLN. INFO.: US 1997-70263P P 19971231
US 1998-223518 A3 19981230
WO 1998-US27644 W 19981230
OTHER SOURCE(S): MARPAT 131:87757
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

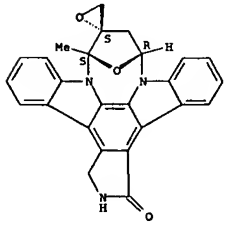
AB Compds. I [R1, R2 = H, alkyl, halo, acyl, NO2, SO3H, CH:NR4, NR5R6, CH(SR7)2, (CH2)jR8, C(:O)NR10R11, OR12, NR10R11, C(:O)R14, S(:O)rR15; R3 = H, alkyl, carbamoyl, NH2, THP, OH, CHO, aralkyl, alkanoyl, CH2CH2R25; R4 = guanidino, heterocyclic, NR5R6; R5 = H, alkyl; R6 = H, alkyl, acyl, aryl, heterocyclyl, carbamoyl, alkylaminocarbonyl; R7 = alkyl, alkylene; j = 1 - 6; R8 = halo, (un)substituted aryl heteroaryl, N3; R9 = H, (un)substituted alkyl, aryl, heteroaryl; R10, R11 = H, (un)substituted alkyl, aryl, heteroaryl, aralkyl, alkylaminocarbonyl, alkoxycarbonyl; R10R11 = heterocyclic; R12 = H, (un)substituted alkyl, aryl, C(:O)R13; R13 = H,

L53 ANSWER 15 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
NR10R11, (un)substituted alkyl, aryl, heteroaryl, aralkyl; R14 = H, (un)substituted alkyl, aryl, heteroaryl; r = 0 - 2; R15 = H, (un)substituted alkyl, aryl, heteroaryl, aralkyl, thiazolinyl, (CH2)aCO2R16; a = 1, 2; R16 = H, alkyl, (CH2)aC(:O)NR10R11; R25 = H, NH2, dialkylamino, OH, hydroxyalkylamino; X = H, CHO, CO2H, alkoxycarbonyl, alkylhydrazinocarbonyl, CN, alkyl,C(:O)NR26R27; R26, R27 = H, H, unsubstituted alkyl, aryl; NR26R27 = heterocycle; Y = H, OH, OC(:O)R33; R33 = alkyl, aryl, NH2, OCH2O-alkyl, O-alkyl, aralkyloxy; XY = CH2OCO2, CHNR16CO2; A1, A2 = H; A1A2 = O; B1, B2 = H; B1B2 = O; where at least one of A1A2 and B1B2 = O and both X and Y .noteq. H] are disclosed. Thus, II was prepd. via treatment of compd. III with BH3 in THF. II displayed pharmacol. activities, including enhancement of function and/or survival of trophic factor responsive cells, inhibition of tyrosine kinase activity [IC50 = 2 nM for trkA kinase], inhibition of VEGF receptor kinase [IC50 = 7 nM] and inhibition of protein kinase C [IC50 = 95. nM].

IT **229983-06-6 229983-08-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of 3'-epimeric k-252a derivs. that enhance the function of cholinergic neurons)

RN 229983-06-6 CAPLUS
CN Spiro[9,12-epoxy-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10(9H),2'-oxiran]-1-one, 2,3,11,12-tetrahydro-9-methyl-, (2'S,9S,12R)- (9CI) (CA INDEX NAME)

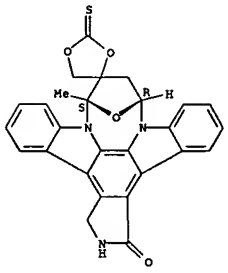
Absolute stereochemistry.



RN 229983-08-8 CAPLUS
CN Spiro[1,3-dioxolane-4,1D'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2',3',11',12'-tetrahydro-9'-methyl-2-thioxo-, (9S,12R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

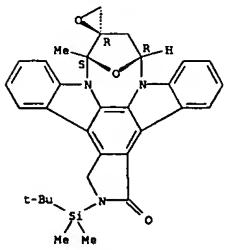
L53 ANSWER 15 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



IT **229976-33-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 3'-epimeric k-252a derivs. that enhance the function of cholinergic neurons)

RN 229976-33-4 CAPLUS
CN Spiro[9,12-epoxy-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10(9H),2'-oxiran]-1-one, 2-[(1,1-dimethylethyl)dimethylsilyl]-2,3,11,12-tetrahydro-9-methyl-, (2'R,9S,12R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

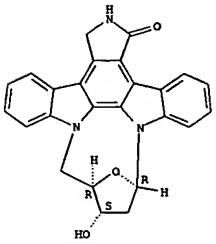
L53 ANSWER 16 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:392535 CAPLUS
DOCUMENT NUMBER: 131:243448
TITLE: Stereocontrolled Total Synthesis of (+)-K252a
AUTHOR(S): Kobayashi, Yoshihisa; Fujimoto, Teppei; Fukuyama, Tohru
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, The University of Tokyo CREST The Japan Science and Technology Corporation (JST), Bunkyo-ku Tokyo, 113-0033, Japan
SOURCE: Journal of the American Chemical Society (1999), 121(27), 6501-6502
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:243448

AB The stereocontrolled total synthesis of (+)-K252a was achieved in 23 steps from indole-3-acetic acid in 10% overall yield.

IT **244128-12-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(stereocontrolled total synthesis of (+)-K252a)

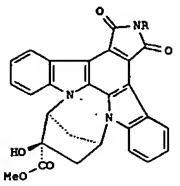
RN 244128-12-9 CAPLUS
CN 9,12-Epoxy-3H,9H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonin-3-one, 1,2,10,11,12,13-hexahydro-11-hydroxy-, (9R,11S,12R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 17 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:320447 CAPLUS
DOCUMENT NUMBER: 131:116392
TITLE: Synthesis of novel carbocyclic analogues of indolocarbazole natural products
AUTHOR(S): Riley, Dean A.; Simpkins, Nigel S.
CORPORATE SOURCE: School of Chemistry, University of Nottingham, University Park, Nottingham, NG7 2RD, UK
SOURCE: Tetrahedron Letters (1999), 40(20), 3929-3932
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:116392
GI



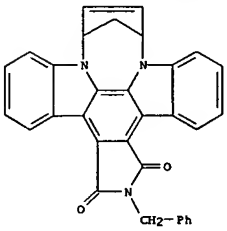
I

AB The synthesis of some cyclopentane-bridged indolocarbazoles, such as I (R = benzyl, H) representing carbocyclic analogs of the natural product K-252a, was achieved by a concise, convergent route, and the ring expansion of one compd. to a staurosporine-type deriv. was also demonstrated. The products are potent inhibitors of protein kinase C (PKC) (no data).

IT **233253-25-3P 233253-26-4P 233253-27-5P**
233253-28-6P 233253-30-0P 233253-31-1P
233253-33-3P 233253-34-4P 233253-35-5P
233253-36-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of novel carbocyclic analogs of staurosporine and K 252a indolocarbazole natural products)

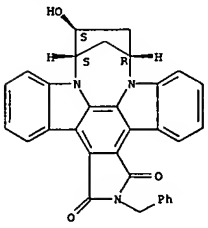
RN 233253-25-3 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-1,3(2H)-dione, 9,12-dihydro-2-(phenylmethyl)- (9CI) (CA INDEX NAME)

L53 ANSWER 17 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



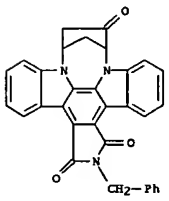
RN 233253-26-4 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-1,3(2H)-dione, 9,10,11,12-tetrahydro-10-hydroxy-2-(phenylmethyl)-, (9R,10R,12S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



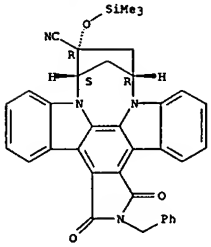
RN 233253-27-5 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-1,3,10(2H,9H)-trione, 11,12-dihydro-2-(phenylmethyl)- (9CI) (CA INDEX NAME)

L53 ANSWER 17 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 233253-28-6 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10-carbonitrile, 2,3,9,10,11,12-hexahydro-1,3-dioxo-2-(phenylmethyl)-10-[(trimethylsilyl)oxy]-, (9R,10S,12S)-rel- (9CI) (CA INDEX NAME)

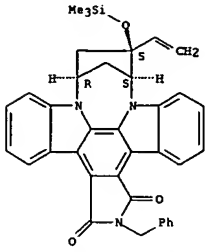
Relative stereochemistry.



RN 233253-30-0 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-1,3(2H)-dione, 10-ethenyl-9,10,11,12-tetrahydro-2-(phenylmethyl)-10-[(trimethylsilyl)oxy]-, (9R,10R,12S)-rel- (9CI) (CA INDEX NAME)

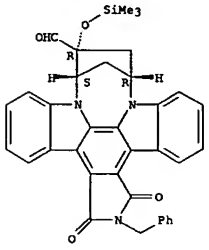
Relative stereochemistry.

L53 ANSWER 17 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



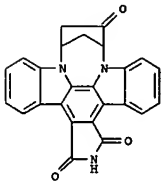
RN 233253-31-1 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10-carboxaldehyde, 2,3,9,10,11,12-hexahydro-1,3-dioxo-2-(phenylmethyl)-10-[(trimethylsilyl)oxy]-, (9R,10S,12S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



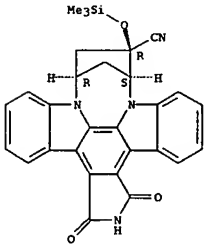
RN 233253-33-3 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-1,3(2H)-dione, 9,12-dihydro- (9CI) (CA INDEX NAME)

L53 ANSWER 17 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 233253-36-6 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10-carbonitrile, 2,3,9,10,11,12-hexahydro-1,3-dioxo-10-[(trimethylsilyl)oxy]-, (9R,10S,12S)-rel- (9CI) (CA INDEX NAME)

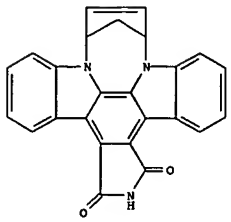
Relative stereochemistry.



IT 233253-29-7P 233253-32-2P 233253-37-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of novel carbocyclic analogs of staurosporine and K 252a indolocarbazole natural products)
RN 233253-29-7 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10-carboxylic acid, 2,3,9,10,11,12-hexahydro-10-hydroxy-1,3-dioxo-2-(phenylmethyl)-, methyl ester, (9R,10S,12S)-rel- (9CI) (CA INDEX NAME)

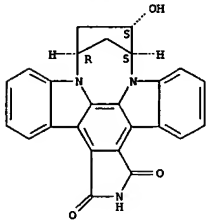
Relative stereochemistry.

L53 ANSWER 17 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



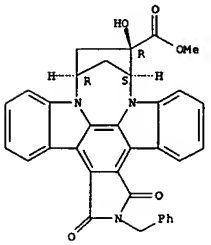
RN 233253-34-4 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-1,3(2H)-dione, 9,10,11,12-tetrahydro-10-hydroxy-, (9R,10R,12S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



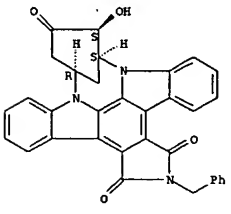
RN 233253-35-5 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-1,3,10(2H,9H)-trione, 11,12-dihydro- (9CI) (CA INDEX NAME)

L53 ANSWER 17 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 233253-32-2 CAPLUS
CN 9,13-Methano-1H,9H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonine-1,3,11(2H,10H)-trione, 12,13-dihydro-10-hydroxy-9-methyl-2-(phenylmethyl)-, (9R,10R,13S)-rel- (9CI) (CA INDEX NAME)

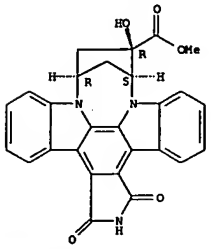
Relative stereochemistry.



RN 233253-37-7 CAPLUS
CN 9,12-Methano-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10-carboxylic acid, 2,3,9,10,11,12-hexahydro-10-hydroxy-1,3-dioxo-, methyl ester, (9R,10S,12S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L53 ANSWER 17 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 18 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1999:304468 CAPLUS
DOCUMENT NUMBER: 130:352261
TITLE: Synthesis of fluorinated macrocyclic bis(indolyl)maleimides as potential 19F NMR probes for protein kinase C
AUTHOR(S): Goekjian, Peter G.; Wu, Guo-Zhang; Chen, Shi; Zhou, Lanxin; Jirousek, Michael R.; Gillig, James R.; Ballas, Lawrence M.; Dixon, Jeffrey T.
CORPORATE SOURCE: Department of Chemistry, Mississippi State University, Mississippi State, MS, 39762, USA
SOURCE: Journal of Organic Chemistry (1999), 64(12), 4238-4246 CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

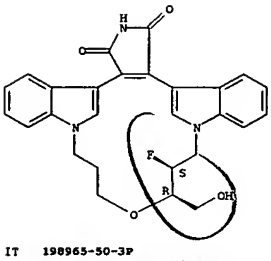
AB Six macrocyclic bis(indolyl)maleimides I, II, and III (X = NMe2, OH) bearing a fluorine label on the aliph. portion of the macrocycle have been prepd. as potential fluorine NMR probes for the catalytic domain of protein kinase C. The macrocyclic bis(indolyl)maleimides such as LY333531 are reversible, ATP competitive, and isoform-selective inhibitors of protein kinase C and may thus serve to probe for subtle differences between protein kinase catalytic domains. The key stereochem. elements were put in place by a Welch aldol condensation between Et fluoroacetate and (R)-cyclohexylidene glyceraldehyde, which was followed by allylation of the secondary alc., elaboration of the alkene and ester to alcs., and mesylation. The macrocycle was formed by slow addn. of a mixt. of the fluorine-labeled aliph. dimesylate and N-Me 2,3-bis[1H-indol-3-yl]maleimide to a suspension of cesium carbonate. Adjusting the functionality led to the six fluorine-labeled macrocyclic bis(indolyl)maleimides. These compds. retain the high potency of the parent compds., with IC50 values below 5 nM for the 14-membered ring compds. I (X = NMe2, OH), II (X = NMe2) and 13-90 nM for the 15-membered ring compds. III. Vicinal proton-fluorine coupling consts. provide an exptl. parameter for detg. the local macrocycle conformation.

IT 198965-49-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and protein kinase C inhibitory activity of macrocyclic bis(indolyl)maleimides)

RN 198965-49-0 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecine-19,21(20H)-dione, 7-fluoro-7,8,11,12-tetrahydro-8-(hydroxymethyl)-, (7S,8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

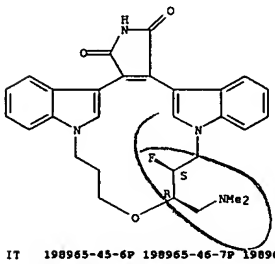
L53 ANSWER 18 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



IT 198965-50-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and protein kinase C inhibitory activity of macrocyclic bis(indolyl)maleimides)

RN 198965-50-3 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecine-19,21(20H)-dione, 8-[(dimethylamino)methyl]-7-fluoro-7,8,11,12-tetrahydro-, (7S,8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

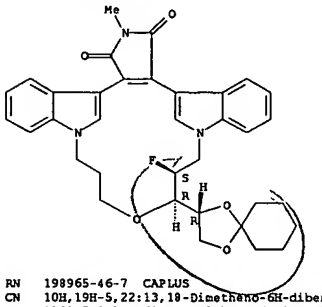


IT 198965-45-6P 198965-46-7P 198965-47-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and protein kinase C inhibitory activity of macrocyclic bis(indolyl)maleimides)

RN 198965-45-6 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecine-19,21(20H)-dione, 8-[(2R)-1,4-dioxaspiro[4.5]dec-2-yl]-7-fluoro-7,8,11,12-tetrahydro-20-methyl-, (7S,8R)- (9CI) (CA INDEX NAME)

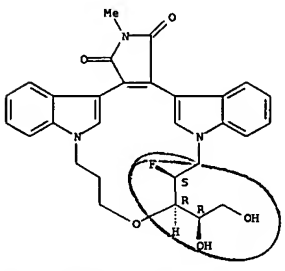
L53 ANSWER 18 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

Absolute stereochemistry.



RN 198965-46-7 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecine-19,21(20H)-dione, 8-[(1R)-1,2-dihydroxyethyl]-7-fluoro-7,8,11,12-tetrahydro-20-methyl-, (7S,8R)- (9CI) (CA INDEX NAME)

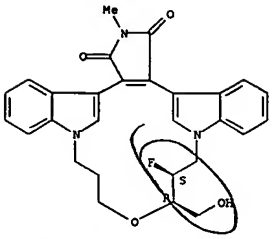
Absolute stereochemistry.



RN 198965-47-8 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecine-19,21(20H)-dione, 7-fluoro-7,8,11,12-tetrahydro-8-(hydroxymethyl)-20-methyl-, (7S,8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L53 ANSWER 18 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 19 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1998:660154 CAPLUS
DOCUMENT NUMBER: 130:3993
TITLE: Synthesis, biochemical and biological evaluation of staurosporine analogs from the microbial metabolite rebeccamycin
AUTHOR(S): Anizon, Fabrice; Moreau, Pascale; Sancelme, Martine; Voldoire, Aline; Prudhomme, Michelle; Ollier, Monique; Severe, Daniele; Riou, Jean-Francois; Bailly, Christian; Fabbro, Doriano; Meyer, Thomas; Aubertin, A. M.
CORPORATE SOURCE: Electrosynthese et Etude de Systemes a Interet Biologique, UMR 6504, Universite Blaise Pascal, Synthese, Aubiere, 63177, Fr.
SOURCE: Bioorganic & Medicinal Chemistry (1998), 6(9), 1597-1604
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

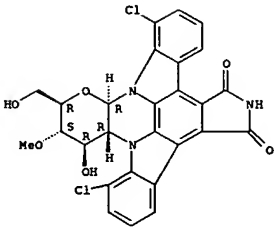
AB The indolo-carbazole antibiotics staurosporine and rebeccamycin are potent antitumor drugs targeting protein kinase C and topoisomerase I, resp. To obtain staurosporine analogs from rebeccamycin, different structural modifications were performed: coupling of the sugar moiety to the second indole nitrogen, dechlorination and then redn. of the imide function to amide. The newly synthesized compds. were tested for their abilities to bind to DNA and to inhibit topoisomerase I and protein kinase C. Their anti-proliferative effects in vitro against B16 melanoma and P388 leukemia (including the related P388CPT cell line resistant to camptothecin) as well as their anti-HIV-1 and antimicrobial activities against various strains of microorganisms were detd. The cytotoxicity of a dechlorinated imide analog correlates well with its DNA binding and anti-topoisomerase I activities. These findings provide guidance for the development of new topoisomerase I-targeted antitumor indolo-carbazoles equipped with a carbohydrate attached to the two indole nitrogens.

IT **215796-56-8P 215796-57-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and biochem. and biol. evaluation of staurosporine analogs from the microbial metabolite rebeccamycin)

RN 215796-56-8 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 4,11-dichloro-5a,8,9,9a-tetrahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aR)- (9CI) (CA INDEX NAME)

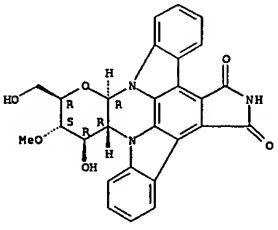
Absolute stereochemistry.

L53 ANSWER 19 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 215796-57-9 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxaline-15,17(16H)-dione, 5a,8,9,9a-tetrahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

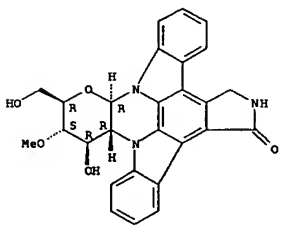


IT **215796-58-0P 215796-59-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and biochem. and biol. evaluation of staurosporine analogs from the microbial metabolite rebeccamycin)

RN 215796-58-0 CAPLUS
CN 7H,15H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxalin-15-one, 5a,8,9,9a,16,17-hexahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aR)- (9CI) (CA INDEX NAME)

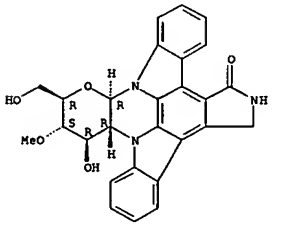
Absolute stereochemistry.

L53 ANSWER 19 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 215796-59-1 CAPLUS
CN 7H,17H-Diindolo[1,2,3-de:3',2',1'-ij]pyrano[2,3-b]pyrrolo[3,4-g]quinoxalin-17-one, 5a,8,9,9a,15,16-hexahydro-9-hydroxy-7-(hydroxymethyl)-8-methoxy-, (5aR,7R,8S,9R,9aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



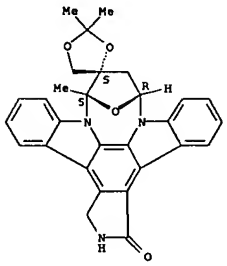
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 20 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:352627 CAPLUS
DOCUMENT NUMBER: 129:54476
TITLE: Protein kinase inhibitors for treatment of neurological disorders
INVENTOR(S): Lewis, Michael E.; Kauer, James C.; Neff, Nicola; Roberts-Lewis, Jill; Murakata, Chikara; Saito, Hiromitsu; Matsuda, Yuzuru; Glicksman, Marcie A.; Kanai, Fumihiko; Kaneko, Masami
PATENT ASSIGNEE(S): Cephalon, Inc., USA; Kyowa Hakko Kogyo Co., Ltd.
SOURCE: U.S., 61 pp., Cont.-in-part of U.S. Ser. No. 329,540.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5756494	A	19980526	US 1995-456642	19950602
US 5461146	A	19951024	US 1993-96561	19930722
EP 768312	A2	19970416	EP 1996-116661	19930726
EP 768312	A3	19970604		
EP 768312	B1	20000906		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
EP 1002534	A1	20000524	EP 1999-120008	19930726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
JP 2003113184	A2	20030418	JP 2002-244111	19930726
US 5621100	A	19970415	US 1994-329540	19941026
CA 2203767	AA	19960509	CA 1995-2203767	19951004
WO 9613506	A1	19960509	WO 1995-US12965	19951004
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9539516	A1	19960523	AU 1995-39516	19951004
AU 704314	B2	19990422		
EP 788501	A1	19970813	EP 1995-937391	19951004
EP 788501	B1	20020605		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
BR 9509480	A	19970930	BR 1995-9480	19951004
JP 10510514	T2	19981013	JP 1996-514605	19951004
EP 1125938	A1	20010822	EP 2001-110483	19951004
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
NZ 295871	A	20010928	NZ 1995-295871	19951004
AT 218571	E	20020615	AT 1995-937391	19951004
ES 2177665	T3	20021216	ES 1995-937391	19951004
US 5741808	A	19980421	US 1997-800383	19970214

PRIORITY APPLN. INFO.: US 1992-920102 B2 19920724
US 1993-96561 A2 19930722
US 1994-329540 A2 19941026
EP 1993-917337 A3 19930726

L53 ANSWER 20 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 20 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

			EP 1996-116661	A3 19930726
			JP 1994-504731	A3 19930726
			US 1995-456642	A 19950602
			EP 1995-937391	A3 19951004
			WO 1995-US12965	W 19951004

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Derivs. of K-252a I (R = HO, MeO; R1 = H, Br, NHCONHPh, CH2SPh, 2-pyrimidinylthiomethyl, 2-furylmethylthiomethyl, etc.; R2 = H, Br, Cl, CH2OH, etc.; R 3 = CH2OH, CO2Me, CH2NHCO2Ph, CONHPh, CH2NHCO2Me, etc.; Z = O, H2), as well as novel bis-N-substituted derivs. of staurosporine XNMeWNMeX (W = C(:Y)NH, W1NHC(:Y); W1 = hydrocarbylene radical of 2-20 carbon atoms; Y = O, S) were prepd. The invention also features a method for treating diseased neuronal cells involving the administration of either the novel staurosporine derivs. or specified functional derivs. of K-252a. Thus, staurosporine was treated with hexamethyl-bis-isocyanate to give 1,6-hexamethylene-bis-(carbamylstaurosporine). The spinal cord choline acetyltransferase (CHAT) activity of I (R = OH, R1 = R2 = Br; R3 = CH2OH, Z = H2) at 300 nM was 146 compared with K-252a of 100.

IT 121664-99-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of staurosporine and K-252a derivs. as protein kinase inhibitors for treatment of neurol. disorders)

RN 121664-99-1 CAPLUS

CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2',3',11',12'-tetrahydro-2,2,9'-trimethyl-, (4S,9'S,12'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L53 ANSWER 21 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:732137 CAPLUS
DOCUMENT NUMBER: 128:13371
TITLE: Preparation of halo-substituted bis-indolemaleimides as protein kinase C inhibitors
INVENTOR(S): Goekjian, Peter G.; Jirousek, Michael R.; Wu, Guo-zhang
PATENT ASSIGNEE(S): Mississippi State University, USA; Eli Lilly and Company
SOURCE: Eur. Pat. Appl., 61 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 805158	A2	19971105	EP 1997-302996	19970501
EP 805158	A3	19980401		
EP 805158	B1	20020116		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
WO 9741127	A1	19971106	WO 1997-US7302	19970430
W: AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, FI, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RU, SD, SG, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9729292	A1	19971119	AU 1997-29292	19970430
AU 703395	B2	19990325		
CN 1223658	A	19990721	CN 1997-195948	19970430
BR 9709301	A	19990810	BR 1997-9301	19970430
US 5936084	A	19990810	US 1997-846272	19970430
JP 11509233	T2	19990817	JP 1997-522343	19970430
JP 3235840	B2	20011204		
NZ 332658	A	20000526	NZ 1997-332658	19970430
AT 212026	E	20020215	AT 1997-302996	19970501
ES 2170918	T3	20020816	ES 1997-302996	19970501
NO 9805080	A	19981208	NO 1998-5080	19981030

PRIORITY APPLN. INFO.: US 1996-16382P P 19960501
WO 1997-US7302 W 19970430

OTHER SOURCE(S): MARPAT 128:13371

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

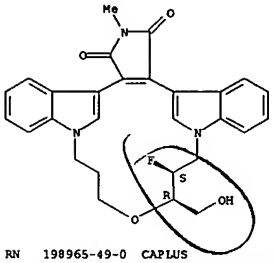
AB The present invention is directed to novel halo-substituted bis-indolemaleimide compds. I [R = H, halogen, OH, alkyl, alkoxy, NR3R4, acylamino; V = O, NH, N-alkyl; T, W = (un)substituted alkylene; J = XC(Y)(S); T = W = CH2, J = (CH2)nCH2C(CH2NR3R4):C(halogen), (CH2)nC(halogen):C(CH2NR3R4)(CH2)m, C(halogen):CHCH(CH2NR3R4)(CH2)n; m, n = 1, 2; X = O, S, bond; Y = halogen, H, alkyl; S = CHO, CZNR2; M = H, CH2OR5, CH2NR3R4, NR3R4; R2 = H, halogen; Z = H, OR6; R3, R4 = H, alkyl, haloalkyl, alkanoyl, haloalkanoly; R3R4 = CR7R8; R7, R8 = H, alkyl, haloalkyl; CR7R8 = cyclopentayl cyclohexyl ring, when Y, S, T or W is a

L53 ANSWER 21 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
halogen or haloalkyl group or when T and W = methylene) and the prepn. of pharmaceutical formulations for use in inhibiting protein kinase C in mammals. Thus, staurosporine analog II was prepd. via condensation of N-methylbis(indol-3-yl)maleimide with dimesylate III. II showed protein kinase C inhibition [IC50 = 1300 nM (vs PKC.alpha.) and IC50 = 90 nM (vs PKC.beta.)].

IT **198965-47-8P 198965-49-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of halo-substituted bis-indolemaleimides as protein kinase C inhibitors)

RN 198965-47-8 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecine-19,21(20H)-dione, 7-fluoro-7,8,11,12-tetrahydro-8-(hydroxymethyl)-20-methyl-, (7S,8R)- (9CI) (CA INDEX NAME)

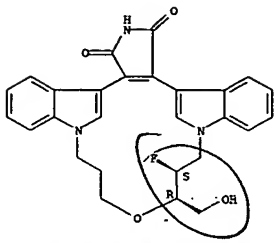
Absolute stereochemistry.



RN 198965-49-0 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecine-19,21(20H)-dione, 7-fluoro-7,8,11,12-tetrahydro-8-(hydroxymethyl)-, (7S,8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

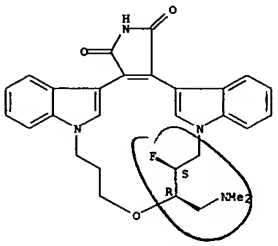
L53 ANSWER 21 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



IT **198965-50-3P 198965-65-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of halo-substituted bis-indolemaleimides as protein kinase C inhibitors)

RN 198965-50-3 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecine-19,21(20H)-dione, 8-{(dimethylamino)methyl}-7-fluoro-7,8,11,12-tetrahydro-, (7S,8R)- (9CI) (CA INDEX NAME)

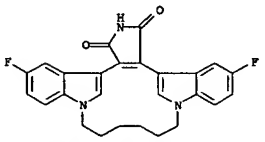
Absolute stereochemistry.



RN 198965-65-0 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 2,15-difluoro-6,7,8,9,10,11-hexahydro- (9CI) (CA INDEX NAME)

Provisional

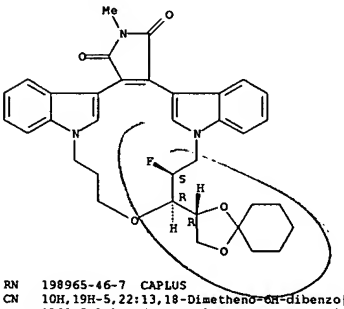
L53 ANSWER 21 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



IT **198965-45-6P 198965-46-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of halo-substituted bis-indolemaleimides as protein kinase C inhibitors)

RN 198965-45-6 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecine-19,21(20H)-dione, 8-[(2R)-1,4-dioxaspiro[4.5]dec-2-yl]-7-fluoro-7,8,11,12-tetrahydro-20-methyl-, (7S,8R)- (9CI) (CA INDEX NAME)

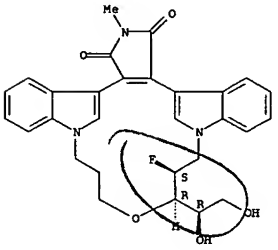
Absolute stereochemistry.



RN 198965-46-7 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecine-19,21(20H)-dione, 8-[(1R)-1,2-dihydroxyethyl]-7-fluoro-7,8,11,12-tetrahydro-20-methyl-, (7S,8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L53 ANSWER 21 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



see 350

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1997:344789 CAPLUS
DOCUMENT NUMBER: 127:17847
TITLE: Staurosporine analogs as protein kinase C inhibitors
INVENTOR(S): Heath, William F., Jr.; Jirousek, Michael R.; Mcdonald, Iii John H.; Rito, Christopher J.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: U.S., 44 pp., Cont.-in-part of U.S. Ser. No. 316,973, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5624949	A	19970429	US 1995-413735	19950330
CA 2137203	AA	19950608	CA 1994-2137203	19941202
FI 9405706	A	19950608	FI 1994-5706	19941202
NO 9404643	A	19950608	NO 1994-4643	19941202
AU 9479188	A1	19950615	AU 1994-79188	19941202
AU 687909	B2	19980305		
BR 9404831	A	19950808	BR 1994-4831	19941202
JP 07215977	A2	19950815	JP 1994-299399	19941202
CN 1111247	A	19951108	CN 1994-119362	19941202
CN 1050844	B	20000329		
HU 71130	A2	19951128	HU 1994-3468	19941202
HU 219709	B	20010628		
RU 2147304	C1	20000410	RU 1994-42922	19941202
TW 425397	B	20010311	TW 1994-83111226	19941202
AT 204579	E	20010915	AT 1994-308947	19941202
PL 182124	B1	20011130	PL 1994-306084	19941202
ES 2162843	T3	20020116	ES 1994-308947	19941202
CZ 291950	B6	20030618	CZ 1994-3018	19941202
BR 9502611	A	19961001	BR 1995-2611	19950531
US 5552396	A	19960903	US 1995-457000	19950601
US 5621098	A	19970415	US 1995-457657	19950601
US 5674862	A	19971007	US 1995-457060	19950601
EP 735038	A1	19961002	EP 1996-302142	19960328
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2216535	AA	19961003	CA 1996-2216535	19960328
CA 2216535	C	20020507		
WO 9630048	A1	19961003	WO 1996-US4245	19960328
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9653249	A1	19961016	AU 1996-53249	19960328
AU 701988	B2	19990211		
CN 1185742	A	19980624	CN 1996-194257	19960328
CN 1093767	B	20021106		
JP 11507327	T2	19990629	JP 1996-529640	19960328
CZ 286301	B6	20000315	CZ 1997-3051	19960328

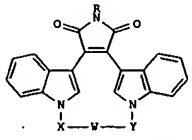
L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PL 183600	B1	20020628	PL 1996-322584	19960328
US 5696108	A	19971209	US 1996-646703	19960506
US 5719175	A	19980217	US 1996-646708	19960506
US 5780461	A	19980714	US 1996-643710	19960506
US 5723456	A	19980303	US 1996-662623	19960613
US 5698578	A	19971216	US 1996-734292	19961021
US 5739322	A	19980414	US 1997-822255	19970320
US 5843935	A	19981201	US 1997-903236	19970712
NO 9704453	A	19971119	NO 1997-4453	19970926
US 5821365	A	19981013	US 1997-971115	19971114
US 6057440	A	20000502	US 1997-970891	19971114
CN 1220266	A	19990623	CN 1997-126094	19971209
CN 1055089	B	20000802		
HK 1013827	A1	20020705	HK 1998-115199	19981223
FI 2000000516	A	20000307	FI 2000-516	20000307
FI 2001001109	A	20010528	FI 2001-1109	20010528

PRIORITY APPLN. INFO.:

US 1993-163060	B2	19931207
US 1994-316973	B2	19941003
US 1995-413735	A3	19950330
US 1995-457060	A1	19950601
US 1995-457657	A3	19950601
WO 1996-US4245	W	19960328
US 1996-643706	A2	19960506
US 1995-643707	B1	19960506
US 1997-822255	A3	19970320

OTHER SOURCE(S): MARPAT 127:17847
GI



I

AB Staurosporine analogs I [R = H, Ac, NH2, OH; W = O, S, SO, SO2, CO, alkylene, (un)substituted NH, NOH, CONH, NHCO, arom., heterocyclic; X, Y = (un)substituted alkylene; and the benzene rings may be further substituted] were prepd. Thus, I [R = H, X = CH2CH2, W = O, Y = (S)-CH(CH2NMe2.HCl)CH2CH2, II] was prepd. from (S)-Me3CSiPh2OCH2CH(OH)CH2CO2Me, Cl3CC(:NH)OCH2CH:CH2, and the diindolylpyrroledione in 8 steps. II had IC50 for protein kinase C.alpha., C.beta.1, and C.beta.2 of 0.36, 0.0047, and 0.0059 .mu.M, resp.

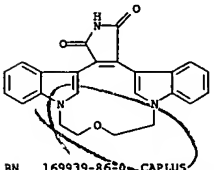
IT 169939-85-9P 169939-86-0P 169939-95-1P
169939-97-3P 169939-99-5P 169940-02-7P
169940-03-8P 169940-04-9P 169940-06-1P

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

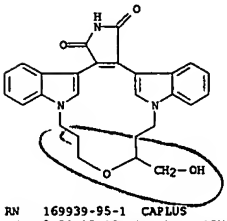
169940-07-2P 169940-08-3P 169940-10-7P
169940-12-9P 169940-13-0P 169940-16-3P
169940-17-4P 169940-18-5P 169940-21-0P
169940-22-1P 169940-24-3P 169940-28-7P
189635-76-5P 189635-81-2P 189635-82-3P
189635-83-4P 189635-84-5P 189635-85-6P
189635-97-0P 189635-98-1P 189636-00-8P
189636-02-0P 189636-03-1P 189636-04-2P
189636-05-3P 189636-06-4P 189636-07-5P
189636-08-6P 189636-09-7P 189636-10-0P
189636-11-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of bridged diindolylpyrroledione as protein kinase C inhibitors)

RN 169939-85-9 CAPLUS
CN 5,20:11,16-Dimetheno-17H-dibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclopentadecine-17,19(18H)-dione, 6,7,9,10-tetrahydro- (9CI) (CA INDEX NAME)

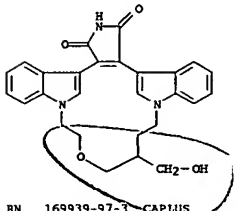


RN 169939-86-0 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecine-19,21(20H)-dione, 7,8,11,12-tetrahydro-8-(hydroxymethyl)- (9CI) (CA INDEX NAME)

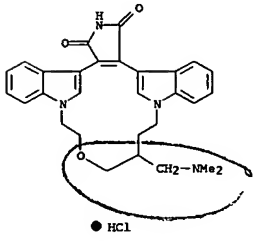


RN 169939-95-1 CAPLUS
CN 5,22:13,18-Dimetheno-19H-dibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacycloheptadecine-19,21(20H)-dione, 6,7,9,10,11,12-hexahydro-10-(hydroxymethyl)- (9CI) (CA INDEX NAME)

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

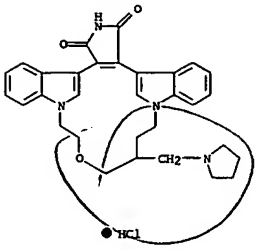


RN 169939-97-3 CAPLUS
CN 5,22:13,18-Dimetheno-19H-dibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacycloheptadecine-19,21(20H)-dione, 10-[(dimethylamino)methyl]-6,7,9,10,11,12-hexahydro-, monohydrochloride (9CI) (CA INDEX NAME)

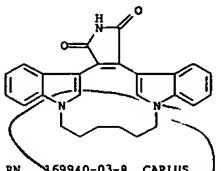


RN 169939-99-5 CAPLUS
CN 5,22:13,18-Dimetheno-19H-dibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacycloheptadecine-19,21(20H)-dione, 6,7,9,10,11,12-hexahydro-10-(1-pyrrolidinylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

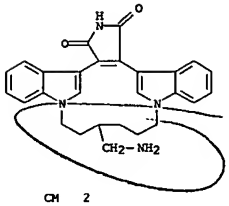


RN 169940-02-7 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro- (9CI) (CA INDEX NAME)



RN 169940-03-8 CAPLUS
CN Carbonic acid, (6,7,8,9,10,11,19,20-octahydro-18,20-dioxo-5,21:12,17-dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecin-8-yl)methyl phenylmethyl ester (9CI) (CA INDEX NAME)

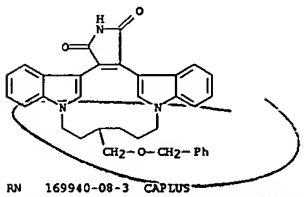
L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



CM 2

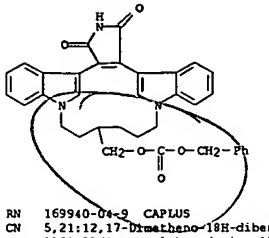
CRN 76-05-1
CMF C2 H F3 O2

RN 169940-07-2 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-[(phenylmethoxy)methyl]- (9CI) (CA INDEX NAME)



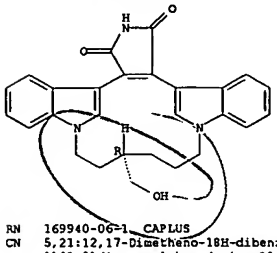
RN 169940-08-3 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-(hydroxymethyl)- (9CI) (CA INDEX NAME)

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 169940-04-9 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-(hydroxymethyl)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

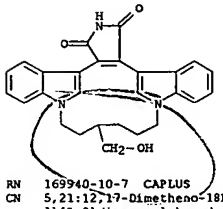


RN 169940-06-1 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-(aminomethyl)-6,7,8,9,10,11-hexahydro-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 169940-05-0
CMF C27 H26 N4 O2

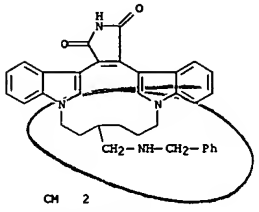
L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 169940-10-7 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-[[(phenylmethyl)amino]methyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 169940-09-4
CMF C34 H32 N4 O2



CM 2

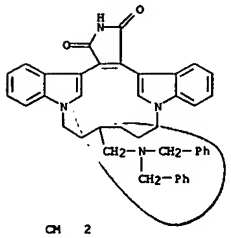
CRN 76-05-1
CMF C2 H F3 O2

RN 169940-12-9 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-[[bis(phenylmethyl)amino]methyl]-6S,7,8,9,10,11-hexahydro-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

CM 1

CRN 169940-11-8
CMF C41 H38 N4 O2



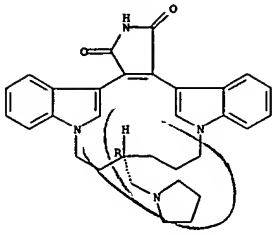
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 169940-13-0 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-(1-pyrrolidinylmethyl)-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

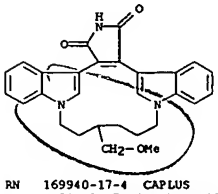
Absolute stereochemistry.

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



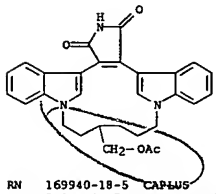
● HCl

RN 169940-16-3 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-(methoxymethyl)- (9CI) (CA INDEX NAME)



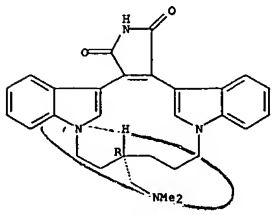
RN 169940-17-4 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-[(acetyloxy)methyl]-6,7,8,9,10,11-hexahydro- (9CI) (CA INDEX NAME)

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 169940-18-5 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-[(dimethylamino)methyl]-6,7,8,9,10,11-hexahydro-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

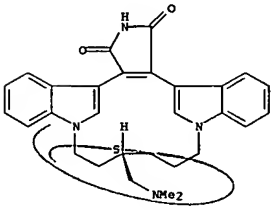


● HCl

RN 169940-21-0 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-[(dimethylamino)methyl]-6,7,8,9,10,11-hexahydro-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

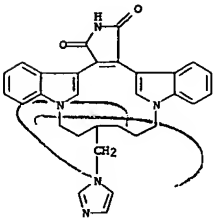
Absolute stereochemistry.

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



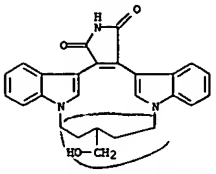
● HCl

RN 169940-22-1 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-(1H-imidazol-1-ylmethyl)- (9CI) (CA INDEX NAME)

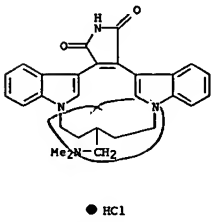


RN 169940-24-3 CAPLUS
CN 6H,17H-5,20:11,16-Dimethenodibenzo[h,n]pyrrolo[3,4-k][1,7]diazacyclopentadecine-17,19(18H)-dione, 7,8,9,10-tetrahydro-8-(hydroxymethyl)- (9CI) (CA INDEX NAME)

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



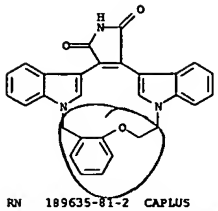
RN 169940-28-7 CAPLUS
CN 6H,17H-5,20:11,16-Dimethenodibenzo[h,n]pyrrolo[3,4-k][1,7]diazacyclopentadecine-17,19(18H)-dione, 8-[(dimethylamino)methyl]-7,8,9,10-tetrahydro-, monohydrochloride (9CI) (CA INDEX NAME)



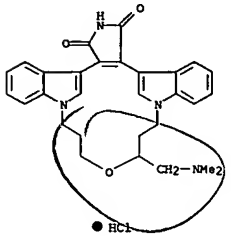
● HCl

RN 189635-76-5 CAPLUS
CN 1H,17H-9,4:18,23-Dimethenotribenzo[e,k,o]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-1,3(2H)-dione, 10,11-dihydro- (9CI) (CA INDEX NAME)

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



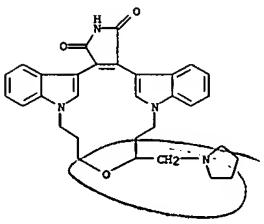
RN 189635-81-2 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecine-19,21(20H)-dione, 8-[(dimethylamino)methyl]-7,8,11,12-tetrahydro-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

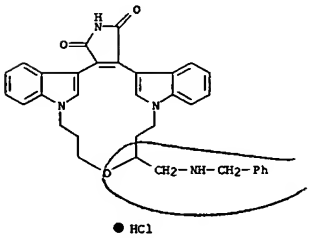
RN 189635-82-3 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecine-19,21(20H)-dione, 7,8,11,12-tetrahydro-8-(1-pyrrolidinylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



● HCl

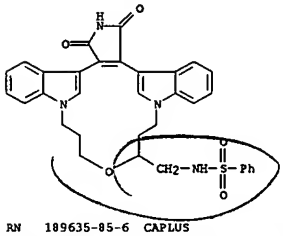
RN 189635-83-4 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecine-19,21(20H)-dione, 7,8,11,12-tetrahydro-8-[[(phenylmethyl)amino]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)



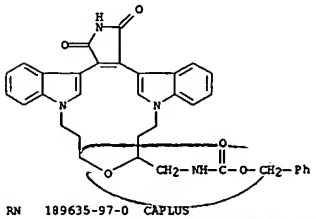
● HCl

RN 189635-84-5 CAPLUS
CN Benzenesulfonamide, N-[(7,8,11,12,20,21-hexahydro-19,21-dioxo-10H,19H-5,22:13,18-dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecin-8-yl)methyl]- (9CI) (CA INDEX NAME)

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

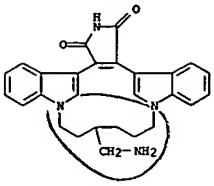


RN 189635-85-6 CAPLUS
CN Carbamic acid, [(7,8,11,12,20,21-hexahydro-19,21-dioxo-10H,19H-5,22:13,18-dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecin-8-yl)methyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



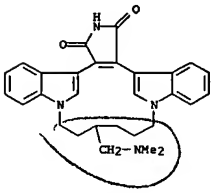
RN 189635-97-0 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-(aminomethyl)-6,7,8,9,10,11-hexahydro-, monohydrochloride (9CI) (CA INDEX NAME)

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



● HCl

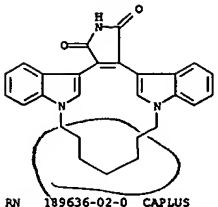
RN 189635-98-1 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-[(dimethylamino)methyl]-6,7,8,9,10,11-hexahydro-, monohydrochloride (9CI) (CA INDEX NAME)



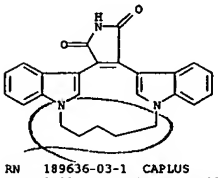
● HCl

RN 189636-00-8 CAPLUS
CN 6H,19H-5,22:13,18-Dimethenodibenzo[j,p]pyrrolo[3,4-m][1,9]diazacycloheptadecine-19,21(20H)-dione, 7,8,9,10,11,12-hexahydro- (9CI) (CA INDEX NAME)

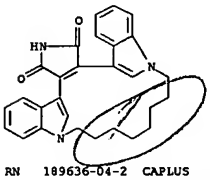
L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 189636-02-0 CAPLUS
CN 6H,17H-5,20:11,16-Dimethenodibenzo[h,n]pyrrolo[3,4-k][1,7]diazacyclopentadecine-17,19(18H)-dione, 7,8,9,10-tetrahydro- (9CI) (CA INDEX NAME)

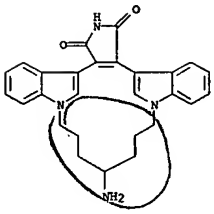


RN 189636-03-1 CAPLUS
CN 5,23:14,19-Dimetheno-20H-dibenzo[b,h]pyrrolo[3,4-e][1,10]diazacyclooctadecine-20,22(21H)-dione, 6,7,8,9,10,11,12,13-octahydro- (9CI) (CA INDEX NAME)

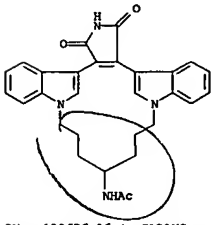


RN 189636-04-2 CAPLUS
CN 6H,19H-5,22:13,18-Dimethenodibenzo[j,p]pyrrolo[3,4-m][1,9]diazacycloheptadecine-19,21(20H)-dione, 9-amino-7,8,9,10,11,12-hexahydro- (9CI) (CA INDEX NAME)

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

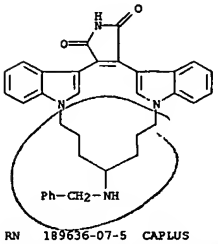


RN 189636-05-3 CAPLUS
CN Acetamide, N-(7,8,9,10,11,12,20,21-octahydro-19,21-dioxo-6H,19H-5,22:13,18-dimethenodibenzo[j,p]pyrrolo[3,4-m][1,9]diazacycloheptadecin-9-yl)- (9CI) (CA INDEX NAME)

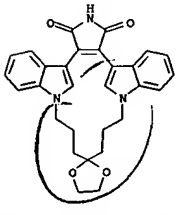


RN 189636-06-4 CAPLUS
CN 6H,19H-5,22:13,18-Dimethenodibenzo[j,p]pyrrolo[3,4-m][1,9]diazacycloheptadecine-19,21(20H)-dione, 7,8,9,10,11,12-hexahydro-9-[(phenylmethyl)amino]- (9CI) (CA INDEX NAME)

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

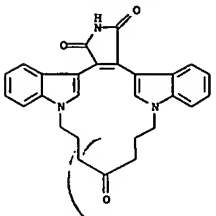


RN 189636-07-5 CAPLUS
CN Spiro[6H,19H-5,22:13,18-dimethenodibenzo[j,p]pyrrolo[3,4-m][1,9]diazacycloheptadecine-9(10H),2'-[1,3]dioxolane]-19,21(20H)-dione, 7,8,11,12-tetrahydro- (9CI) (CA INDEX NAME)

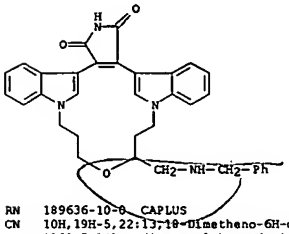


RN 189636-08-6 CAPLUS
CN 6H,19H-5,22:13,18-Dimethenodibenzo[j,p]pyrrolo[3,4-m][1,9]diazacycloheptadecine-9,19,21(10H,20H)-trione, 7,8,11,12-tetrahydro- (9CI) (CA INDEX NAME)

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

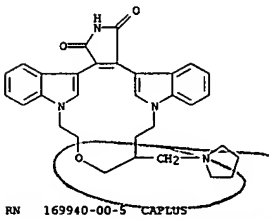


RN 189636-09-7 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecine-19,21(20H)-dione, 7,8,11,12-tetrahydro-8-[[(phenylmethyl)amino]methyl]- (9CI) (CA INDEX NAME)



RN 189636-10-0 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecine-19,21(20H)-dione, 8-(aminomethyl)-7,8,11,12-tetrahydro- (9CI) (CA INDEX NAME)

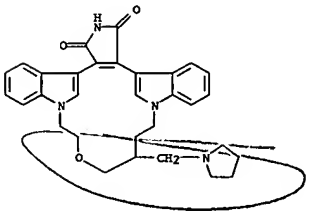
L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 169940-00-5 CAPLUS
CN 5,22:13,18-Dimetheno-19H-dibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacycloheptadecine-19,21(20H)-dione, 6,7,9,10,11,12-hexahydro-10-(1-pyrrolidinylmethyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 169939-96-2
CMF C31 H32 N4 O3

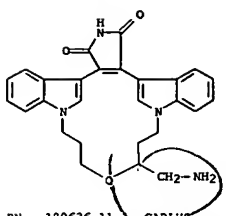


CM 2

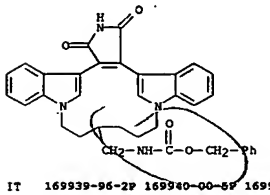
CRN 76-05-1
CMF C2 H F3 O2

RN 169940-19-6 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 189636-11-1 CAPLUS
CN Carbamic acid, [(6,7,8,9,10,11,19,20-octahydro-18,20-dioxo-5,21:12,17-dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecin-8-yl)methyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

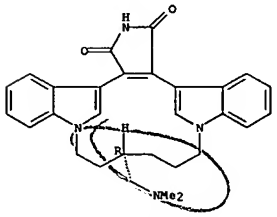


IT 169939-96-2P 169940-00-5P 169940-19-6P
169940-40-3P 169940-81-2P 169940-86-7P
169940-88-9P 169940-90-3P 169940-94-7P
169940-96-9P 169940-98-1P 169941-01-9P
169941-06-4P 169941-10-0P 169941-12-2P
189635-79-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of bridged diindolylpyrrolediones as protein kinase C inhibitors)

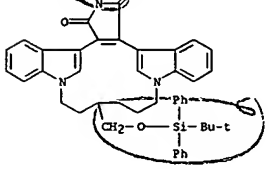
RN 169939-96-2 CAPLUS
CN 5,22:13,18-Dimetheno-19H-dibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacycloheptadecine-19,21(20H)-dione, 6,7,9,10,11,12-hexahydro-10-(1-pyrrolidinylmethyl)- (9CI) (CA INDEX NAME)

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-[(dimethylamino)methyl]-6,7,8,9,10,11-hexahydro-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

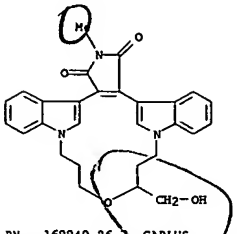


RN 169940-40-3 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-6,7,8,9,10,11-hexahydro-19-methyl- (9CI) (CA INDEX NAME)

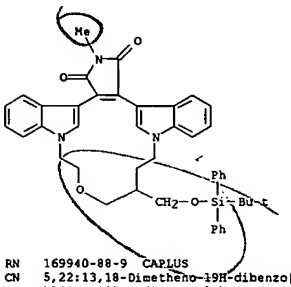


RN 169940-81-2 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecine-19,21(20H)-dione, 7,8,11,12-tetrahydro-8-(hydroxymethyl)-20-methyl- (9CI) (CA INDEX NAME)

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

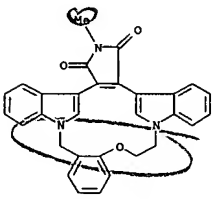


RN 169940-86-7 CAPLUS
CN 5,22:13,18-Dimetheno-19H-dibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacycloheptadecine-19,21(20H)-dione, 10-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-6,7,9,10,11,12-hexahydro-20-methyl- (9CI) (CA INDEX NAME)

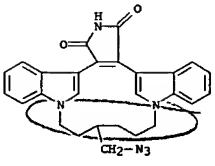


RN 169940-88-9 CAPLUS
CN 5,22:13,18-Dimetheno-19H-dibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacycloheptadecine-19,21(20H)-dione, 6,7,9,10,11,12-hexahydro-10-[[(methylsulfonyl)oxy]methyl]- (9CI) (CA INDEX NAME)

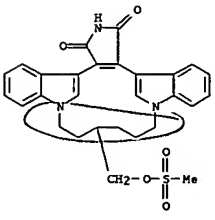
L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 169940-96-9 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-(azidomethyl)-6,7,8,9,10,11-hexahydro- (9CI) (CA INDEX NAME)

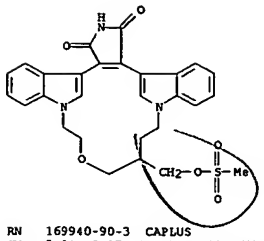


RN 169940-98-1 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-[[(methylsulfonyl)oxy]methyl]- (9CI) (CA INDEX NAME)

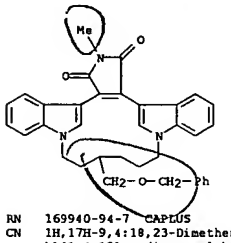


RN 169941-01-9 CAPLUS

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

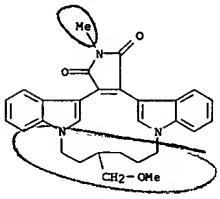


RN 169940-90-3 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-19-methyl-8-[(phenylmethoxy)methyl]- (9CI) (CA INDEX NAME)

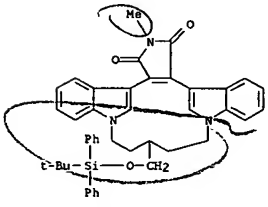


RN 169940-94-7 CAPLUS
CN 1H,17H-9,4:18,23-Dimethenotribenzo[e,k,o]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-1,3(2H)-dione, 10,11-dihydro-2-methyl- (9CI) (CA INDEX NAME)

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-(methoxymethyl)-19-methyl- (9CI) (CA INDEX NAME)

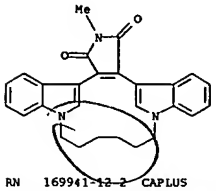


RN 169941-06-4 CAPLUS
CN 6H,17H-5,20:11,16-Dimethenodibenzo[h,n]pyrrolo[3,4-k][1,7]diazacyclopentadecine-17,19(18H)-dione, 8-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-7,8,9,10-tetrahydro-18-methyl- (9CI) (CA INDEX NAME)



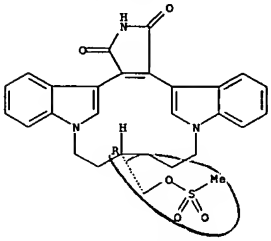
RN 169941-10-0 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-19-methyl- (9CI) (CA INDEX NAME)

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



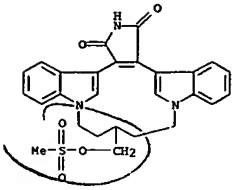
RN 169941-12-2 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-[[(methylsulfonyl)oxy]methyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



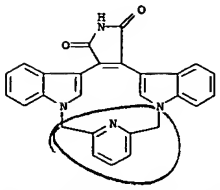
RN 189635-79-8 CAPLUS
CN 6H,17H-5,20:11,16-Dimethenodibenzo[h,n]pyrrolo[3,4-k][1,7]diazacyclopentadecine-17,19(18H)-dione, 7,8,9,10-tetrahydro-8-[[(methylsulfonyl)oxy]methyl]- (9CI) (CA INDEX NAME)

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



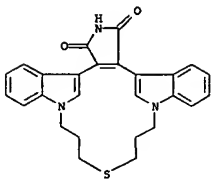
IT 169940-01-6P 169940-23-2P 169940-26-5P
169941-13-3P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of bridged diindolylpyrrolediones as protein kinase C inhibitors)

RN 169940-01-6 CAPLUS
CN 6H,12H,19H-5,22:13,18-Dimetheno-7,11-nitrilodibenzo[j,p]pyrrolo[3,4-m][1,9]diazacycloheptadecine-19,21(20H)-dione (9CI) (CA INDEX NAME)

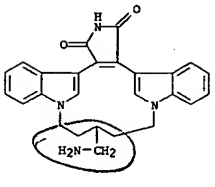


RN 169940-23-2 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]thiadiazacycloheptadecine-19,21(20H)-dione, 7,8,10,11-tetrahydro- (9CI) (CA INDEX NAME)

L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 169940-26-5 CAPLUS
CN 6H,17H-5,20:11,16-Dimethenodibenzo[h,n]pyrrolo[3,4-k][1,7]diazacyclopentadecine-17,19(18H)-dione, 8-(aminomethyl)-7,8,9,10-tetrahydro-, monohydrochloride (9CI) (CA INDEX NAME)

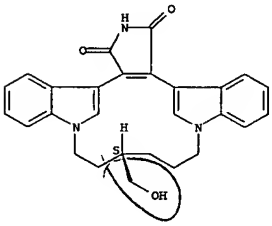


● HCl

RN 169941-13-3 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-(hydroxymethyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

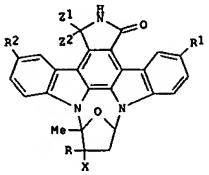
L53 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



L53 ANSWER 23 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:276796 CAPLUS
DOCUMENT NUMBER: 126:343709
TITLE: Protein kinase inhibitors for treatment of neurological disorders
INVENTOR(S): Lewis, Michael E.; Kauer, James C.; Neff, Nicola; Roberts-Lewis, Jill; Murakata, Chikara; Saito, Hiromitsu; Matsuda, Yuzuru; Glicksman, Marcie A.; Kanai, Fumihiko; Kaneko, Masami
PATENT ASSIGNEE(S): Cephalon, Inc., USA; Kyowa Hakko Kogyo
SOURCE: U.S., 60 pp., Cont.-in-part of U.S. 5,621,100.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5621101	A	19970415	US 1995-486739	19950607
US 5461146	A	19951024	US 1993-96561	19930722
EP 768312	A2	19970416	EP 1996-116661	19930726
EP 768312	A3	19970604		
EP 768312	B1	20000906		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
EP 1002534	A1	20000524	EP 1999-120008	19930726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
JP 2003113184	A2	20030418	JP 2002-244111	19930726
US 5621100	A	19970415	US 1994-329540	19941026

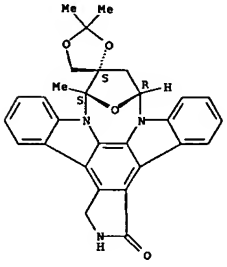
PRIORITY APPLN. INFO.: US 1992-920102 B2 19920724
US 1993-96561 A2 19930722
US 1994-329540 A2 19941026
EP 1993-917337 A3 19930726
EP 1996-116661 A3 19930726
JP 1994-504731 A3 19930726
OTHER SOURCE(S): MARPAT 126:343709
GI



I

L53 ANSWER 23 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
AB K-252a derivs., e.g. I [R = OH; R1 = H, CH2SO2Et, CH2SCH2CH2NH2, (1,3,5-triazol-1-yl)iminomethyl, CH2SCH2CH2NHBu, CH2CH2CH2NMe2, CH2NMe2, 2-pyridylthiomethyl, 2-pyrimidinylthiomethyl, 2-pyrimidinylsulfinylmethyl; R2 = Z1 = Z2 = H; X = CH2NHCOCH(CH2OH)NHCbz-(S), CO2Me, CONH2], were prepd. as protein kinase inhibitors for treatment of neurol. disorders. I (R = OH, R1 = CH2SO2Et, R2 = Z1 = Z2 = H, X = CO2Me; (II)] was prepd. from I (R = OH, R1 = CH2SEt, R2 = Z1 = Z2 = H, X = CO2Me) via oxidn. with 3-ClC6H4CO3H in CHCl3. II at 30 nM had an Ipsi/Contra ratio of 62 for cortical ChAT activity in NBM rats with lesions.
IT 121664-99-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of K-252a derivs. as protein kinase inhibitors for treatment of neurol. disorders)
RN 121664-99-1 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2',3',11',12'-tetrahydro-2,2,9'-trimethyl-, (4S,9'S,12'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L53 ANSWER 24 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:276795 CAPLUS
DOCUMENT NUMBER: 126:343708
TITLE: K-252a derivatives for treatment of neurological disorders
INVENTOR(S): Saito, Hiromitsu; Matsuda, Yuzuru; Glicksman, Marcie A.; Kanai, Fumihiko; Kaneko, Masami; Lewis, Michael E.; Kauer, James C.; Neff, Nicola; Roberts-Lewis, Jill; Murakata, Chikara
PATENT ASSIGNEE(S): Cephalon, Inc., USA; Kyowa Hakko Kogyo Co., Ltd.
SOURCE: U.S., 51 pp., Cont.-in-part of U.S. 5,461,146.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5621100	A	19970415	US 1994-329540	19941026
US 5461146	A	19951024	US 1993-96561	19930722
EP 768312	A2	19970416	EP 1996-116661	19930726
EP 768312	A3	19970604		
EP 768312	B1	20000906		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
EP 1002534	A1	20000524	EP 1999-120008	19930726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
JP 2003113184	A2	20030418	JP 2002-244111	19930726
US 5756494	A	19980526	US 1995-456642	19950602
US 5621101	A	19970415	US 1995-486739	19950607
CA 2203767	AA	19960509	CA 1995-2203767	19951004
WO 9613506	A1	19960509	WO 1995-US12965	19951004
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9539516	A1	19960523	AU 1995-39516	19951004
AU 704314	B2	19990422		
EP 788501	A1	19970813	EP 1995-937391	19951004
EP 788501	B1	20020605		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
BR 9509480	A	19970930	BR 1995-9480	19951004
JP 10510514	T2	19981013	JP 1996-514605	19951004
EP 1125938	A1	20010822	EP 2001-110483	19951004
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
NZ 295871	A	20010928	NZ 1995-295871	19951004
AT 218571	E	20020615	AT 1995-937391	19951004
ES 2177665	T3	20021216	ES 1995-937391	19951004
US 5741808	A	19980421	US 1997-800383	19970214

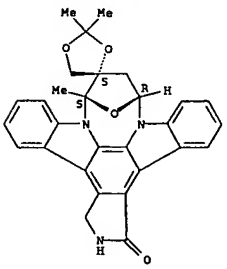
PRIORITY APPLN. INFO.: US 1992-920102 B2 19920724
US 1993-96561 A2 19930722
EP 1993-917337 A3 19930726
EP 1996-116661 A3 19930726
JP 1994-504731 A3 19930726
US 1994-329540 A2 19941026
US 1995-456642 A 19950602

L53 ANSWER 24 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
EP 1995-937391 A3 19951004
WO 1995-US12965 W 19951004
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB K-252a derivs. were prepd. as agents for treatment of neurol. disorders. The deriv. I is claimed. I was prepd. from from dialdehyde II via redn. with NaBH4, thiolation with EtSH in the presence of CSA, and deacetylation with NaOMe. I (0.03 mg/kg QOD) had an Ipsi/Contra ratio of 93.8 for cortical ChAT activity in NBM rats with lesions.
IT 121664-99-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of K-252a derivs. as protein kinase inhibitors for treatment of neurol. disorders)
RN 121664-99-1 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2',3',11',12'-tetrahydro-2,2,9'-trimethyl-, (4S,9'S,12'R)- (9CI) (CA INDEX NAME)

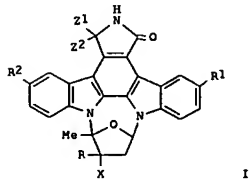
Absolute stereochemistry.



L53 ANSWER 25 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:124905 CAPLUS
DOCUMENT NUMBER: 126:216650
TITLE: Aqueous polyethylene glycol solutions containing indolocarbazoles
INVENTOR(S): Goldstein, Joel D.; Herman, Joseph L.
PATENT ASSIGNEE(S): Cephalon, Inc., USA
SOURCE: U.S., 31 pp., Cont.-in-part of U.S. Ser. No. 199,390, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5599808	A	19970204	US 1995-383414	19950203
PRIORITY APPLN. INFO.:			US 1994-199390	19940218

GI



I

AB Solns. of indolocarbazoles, such as I [R = OH, OMe; R1 = H, Br, Cl, Me, NHCONHPh, CH2S(O)nEt, NMe2, NHCO2Me, CH2OCONHEt, CH2OEt, CH2NMe2, CH2SEt, CH:NNH; R2 = H, Br, Cl, NHCONHEt, CH2SEt, CH2OH; X = H, CH2N3, CO2Me, CH2OH, CONHEt, CONH2, CONHPr,CH2S(O)Me, CH:NOH, CONHCH2CH2OH, CH:NNHCONH2, CH2OAc, CONHPh, CH2S(O)nPh; Z1 = Z2 = H; Z1Z2 = O; n = 0-2], contain 1-99% org. solvent, 0.25-10% dispersant, 0-99% H2O and 0-60% polyethylene glycol. Thus, K-252a was dissolved in a solvent contg. 50% PEG-600, 2% benzyl alc., 10% Triton X-100 and 38% H2O to give a soln. contg. 10 mg/mL K-252a. Many I were also prepd.

IT **121665-38-1 121679-09-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of aq. polyethylene glycol solns. contg. indolocarbazoles)

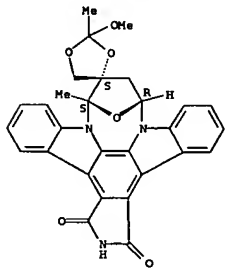
RN 121665-38-1 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2',3',11',12'-tetrahydro-2-methoxy-2,9'-dimethyl-, (4S,9'S,12'R)- (9CI) (CA INDEX NAME)

L53 ANSWER 25 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

(Reactant or reagent)
(prepn. of aq. polyethylene glycol solns. contg. indolocarbazoles)

RN 122605-43-0 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine]-1',3'(2'H)-dione, 11',12'-dihydro-2-methoxy-2,9'-dimethyl-, (4S,9'S,12'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



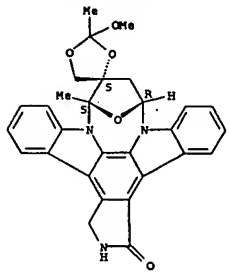
IT **170719-69-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of aq. polyethylene glycol solns. contg. indolocarbazoles)

RN 170719-69-4 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine]-1',3'(2'H)-dione, 2'-amino-11',12'-dihydro-2,2,9'-trimethyl-, [9'S-(9'.alpha.,10'.alpha.,12'.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

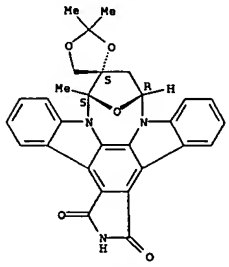
L53 ANSWER 25 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

Absolute stereochemistry.



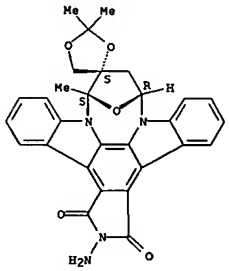
RN 121679-09-2 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine]-1',3'(2'H)-dione, 11',12'-dihydro-2,2,9'-trimethyl-, [9'S-(9'.alpha.,10'.beta.,12'.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **122605-43-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

L53 ANSWER 25 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



L53 ANSWER 26 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:51850 CAPLUS
DOCUMENT NUMBER: 126:144299
TITLE: Preparation of diindolo compounds as antitumor agents
INVENTOR(S): Vice, Susan F.
PATENT ASSIGNEE(S): Vice; Susan F., USA
SOURCE: U.S., 35 pp., Cont.-in-part of U.S. Ser. No. 951,052, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5589472	A	19961231	US 1995-397205	19950310
WO 9407895	A1	19940414	WO 1993-US8276	19930909

W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, VN
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1992-951052 B2 19920925
WO 1993-US8276 W 19930909
OTHER SOURCE(S): MARPAT 126:144299
GI

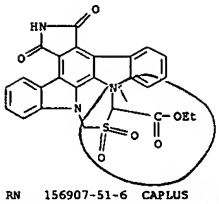
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; X, Y = O, NH, H2, (H,OH); R1, R2 = H, OH, Cl, F, MeO, Me; Z = O, S, SO, SO2; R3, R4 = H, (CH2)pOH (wherein p = 1-2), etc.], useful for the treatment of inflammation, tumors and psoriasis, were prepd. and formulated. Thus, reaction of 11,12-dicyanoindolocarbazole II with HCHO and MeNH2 in AcOH/H2O followed by treatment of the intermediate III in DMSO with KOH/H2O, and treatment of the resulting compd. IV with TFA in DMSO/H2O afforded V which showed IC50 of 90 nM against protein kinase C.

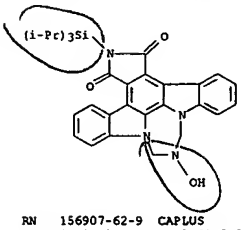
IT 156907-36-7P 156907-40-3P 156907-42-5P
156907-48-1P 156907-51-6P 156907-62-9P
156907-63-0P 156907-64-1P 157018-71-8P
157018-72-9P 157018-77-4P 157018-78-5P
157018-81-0P 157018-83-2P 186583-88-0P
186583-90-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of diindolo compds. as antitumor agents)

RN 156907-36-7 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',1',2'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepine-1,3(2H)-dione, 10,11-dihydro-10-methyl- (9CI) (CA INDEX NAME)

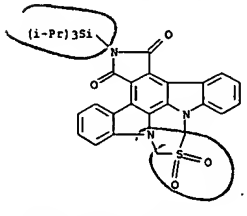
L53 ANSWER 26 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 156907-51-6 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',1',2'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepine-1,3(2H)-dione, 10,11-dihydro-10-hydroxy-2-[tris(1-methylethyl)silyl]- (9CI) (CA INDEX NAME)

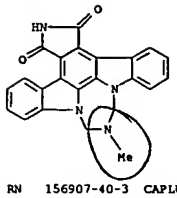


RN 156907-62-9 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 2-[tris(1-methylethyl)silyl]-, 10,10-dioxide (9CI) (CA INDEX NAME)

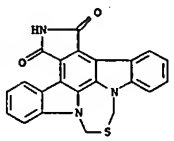


RN 156907-63-0 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 9,11-dimethyl-2-[tris(1-methylethyl)silyl]-, 10,10-dioxide, cis- (9CI) (CA INDEX NAME)

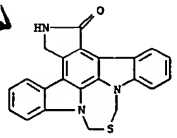
L53 ANSWER 26 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 156907-40-3 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione (9CI) (CA INDEX NAME)



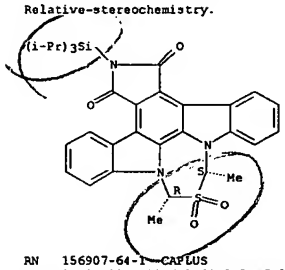
RN 156907-42-5 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepin-1-one, 2,3-dihydro- (9CI) (CA INDEX NAME)



RN 156907-48-1 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-9-carboxylic acid, 2,3-dihydro-1,3-dioxo-, ethyl ester, 10,10-dioxide (9CI) (CA INDEX NAME)

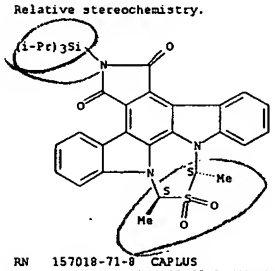
L53 ANSWER 26 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

Relative-stereochemistry.



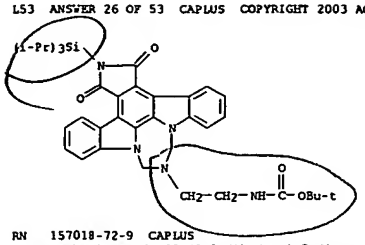
RN 156907-64-1 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 9,11-dimethyl-2-[tris(1-methylethyl)silyl]-, 10,10-dioxide, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

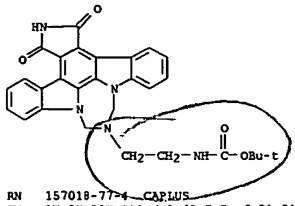


RN 157018-71-8 CAPLUS
CN Carbamic acid, [2-[2,3-dihydro-1,3-dioxo-2-[tris(1-methylethyl)silyl]-1H,9H-diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepin-10(11H)-yl]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

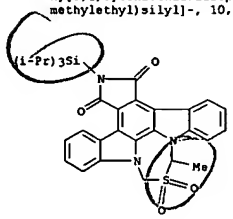
L53 ANSWER 26 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



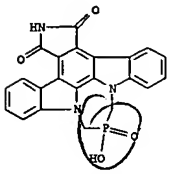
RN 157018-72-9 CAPLUS
CN Carbamic acid, [2-(2,3-dihydro-1,3-dioxo-1H,9H-diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepin-10(11H)-yl)ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



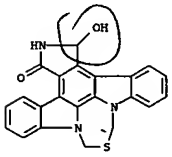
RN 157018-77-4 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 9-methyl-2-[tris(1-methylethyl)silyl]-, 10,10-dioxide (9CI) (CA INDEX NAME)



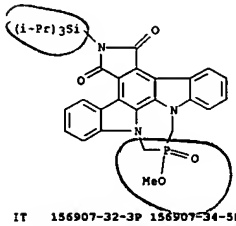
L53 ANSWER 26 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 186583-88-0 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepin-1-one, 2,3-dihydro-3-hydroxy- (9CI) (CA INDEX NAME)

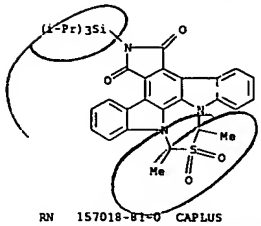


RN 186583-90-4 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][1,5,3]benzodiazaphosphepine-1,3(2H)-dione, 10,11-dihydro-10-methoxy-2-[tris(1-methylethyl)silyl]-, 10-oxide (9CI) (CA INDEX NAME)

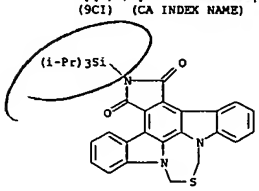


IT 156907-32-3P 156907-34-5P 156907-35-6P
156907-43-6P 156907-44-7P 156907-45-8P
156907-46-9P 156907-47-0P 156907-65-2P
157018-73-0P 157018-74-1P 157018-79-6P
157018-80-9P 157018-84-3P 186583-91-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

L53 ANSWER 26 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
RN 157018-78-5 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 9,11-dimethyl-2-[tris(1-methylethyl)silyl]-, 10,10-dioxide (9CI) (CA INDEX NAME)

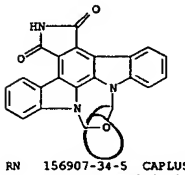


RN 157018-81-0 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 2-[tris(1-methylethyl)silyl]- (9CI) (CA INDEX NAME)

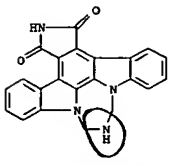


RN 157018-83-2 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][1,5,3]benzodiazaphosphepine-1,3(2H)-dione, 10,11-dihydro-10-hydroxy-, 10-oxide (9CI) (CA INDEX NAME)

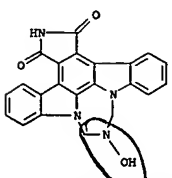
L53 ANSWER 26 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of diindolo compds. as antitumor agents)
RN 156907-32-3 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzoxadiazepine-1,3(2H)-dione (9CI) (CA INDEX NAME)



RN 156907-34-5 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',1',2'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepine-1,3(2H)-dione, 10,11-dihydro- (9CI) (CA INDEX NAME)

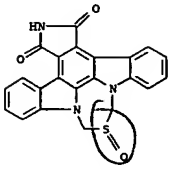


RN 156907-35-6 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',1',2'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepine-1,3(2H)-dione, 10,11-dihydro-10-hydroxy- (9CI) (CA INDEX NAME)

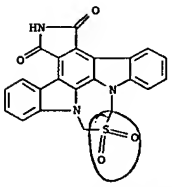


RN 156907-43-6 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 10-oxide (9CI) (CA INDEX NAME)

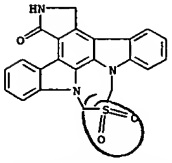
L53 ANSWER 26 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 156907-44-7 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 10,10-dioxide (9CI) (CA INDEX NAME)

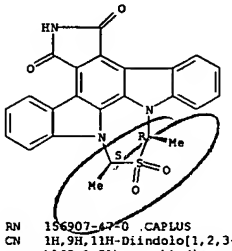


RN 156907-45-8 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepin-1-one, 2,3-dihydro-, 10,10-dioxide (9CI) (CA INDEX NAME)



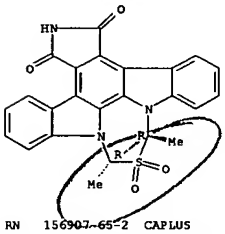
RN 156907-46-9 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 9,11-dimethyl-, 10,10-dioxide, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



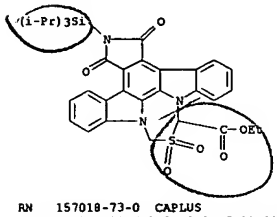
RN 156907-47-0 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 9,11-dimethyl-, 10,10-dioxide, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

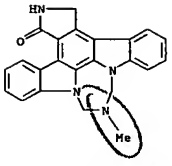


RN 156907-65-2 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-9-carboxylic acid, 2,3-dihydro-1,3-dioxo-2-[tris(1-methylethyl)silyl]-, ethyl ester, 10,10-dioxide (9CI) (CA INDEX NAME)

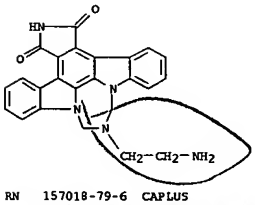
L53 ANSWER 26 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 157018-73-0 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepin-1-one, 2,3,10,11-tetrahydro-10-methyl- (9CI) (CA INDEX NAME)

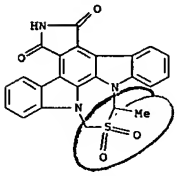


RN 157018-74-1 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',1',2'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepine-1,3(2H)-dione, 10-(2-aminoethyl)-10,11-dihydro- (9CI) (CA INDEX NAME)

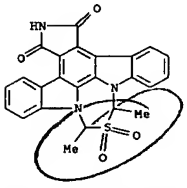


RN 157018-79-6 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 9-methyl-, 10,10-dioxide (9CI) (CA INDEX NAME)

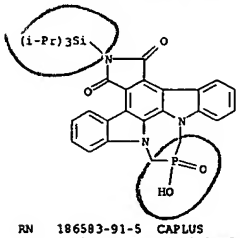
L53 ANSWER 26 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 157018-80-9 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 9,11-dimethyl-, 10,10-dioxide (9CI) (CA INDEX NAME)

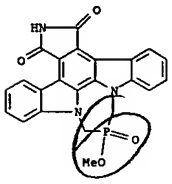


RN 157018-84-3 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][1,5,3]benzodiazaphosphepine-1,3(2H)-dione, 10,11-dihydro-10-hydroxy-2-[tris(1-methylethyl)silyl]-, 10-oxide (9CI) (CA INDEX NAME)



RN 186583-91-5 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][1,5,3]benzodiazaphosphepine-1,3(2H)-dione, 10,11-dihydro-10-methoxy-, 10-oxide (9CI) (CA INDEX NAME)

L53 ANSWER 26 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

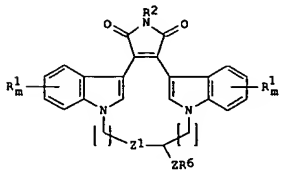


L53 ANSWER 27 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1996:685338 CAPLUS
DOCUMENT NUMBER: 125:328740
TITLE: Preparation of bis(indolo)macrocycles as protein kinase C inhibitors
INVENTOR(S): Heath, William Francis, Jr.; Jirousek, Michael Robert; McDonald, John Hampton; Rito, Christopher John
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 735038	A1	19961002	EP 1996-302142	19960328
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5624949	A	19970429	US 1995-413735	19950330

PRIORITY APPLN. INFO.: US 1995-413735 A 19950330
US 1993-163060 B2 19931207
US 1994-316973 B2 19941003
OTHER SOURCE(S): MARPAT 125:328740
GI



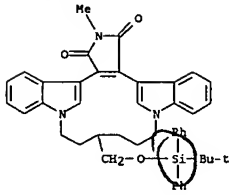
I

AB Title compds. [I; R1 = H, halo, alkyl, alkoxy, etc.; R2 = H, OH, NH2, Ac; R6 = NHCF3, NMeCF3; Z = (CH2)p, (CH2)pO(CH2)p; Z1 = O, S, NH; m = 0-3; p = 0-2] were prepd. I had IC50 of <100.mu.M against protein kinase C.

IT 169940-40-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of bis(indolo)macrocycles as protein kinase C inhibitors)

RN 169940-40-3 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-6,7,8,9,10,11-hexahydro-19-methyl- (9CI) (CA INDEX NAME)

L53 ANSWER 27 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



L53 ANSWER 28 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1996:610363 CAPLUS
DOCUMENT NUMBER: 125:247615
TITLE: Synthesis of macrocyclic bisindolylmaleimides via intramolecular McMurry coupling
INVENTOR(S): Gillig, James R.; Jirousek, Michael R.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: U.S., 9 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5559228	A	19960924	US 1995-413311	19950330
CA 2216633	AA	19961003	CA 1996-2216633	19960327
CA 2216633	C	20020813		
WO 9630348	A1	19961003	WO 1996-US4437	19960327
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
AU 9653816	A1	19961016	AU 1996-53816	19960327
EP 820446	A1	19980128	EP 1996-910688	19960327
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE				
JP 11502857	T2	19990309	JP 1996-529734	19960327
JP 3014146	B2	20000228		

PRIORITY APPLN. INFO.: US 1995-413311 A 19950330
WO 1996-US4437 W 19960327
OTHER SOURCE(S): CASREACT 125:247615; MARPAT 125:247615
GI

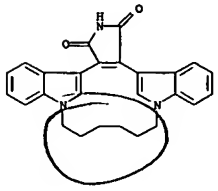
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention provides an efficient process of reacting a bisindole acid or ester I [R1 = H, C1-4 alkyl, PhCH2; R, X, Y = optional substituents] with low-valent Ti to produce a bisindolylmaleic acid deriv. II. Compds. II are readily converted to the title bisindolylmaleimides III, which are known and potent inhibitors of protein kinase C (no data). For example, coupling of 2 mol indole with 1 mol Br(CH2)6Br gave 96% 1,6-bis(1-indolyl)hexane, which reacted with oxalyl chloride and then MeOH to give 80% I [R = H, R1 = Me, XY = (CH2)6]. Intramol. coupling of the latter using Zn-Cu couple and TiCl3 in DME/THF/CH2Cl2 at room temp. gave 48% II [groups as above]. This ester was hydrolyzed with NaOH in aq. MeOH/dioxane, followed by acidification, to give 73% of the corresponding cyclic anhydride. Treatment of the anhydride with (Me3Si)2NH and MeOH in DMF gave III [R = H, XY = (CH2)6], also in 73% yield.

IT 169940-02-7P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of macrocyclic bisindolylmaleimides via intramol. McMurry coupling)

RN 169940-02-7 CAPLUS

L53 ANSWER 28 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro- (9CI) (CA INDEX NAME)

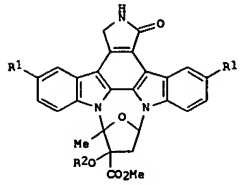


L53 ANSWER 29 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:404877 CAPLUS
DOCUMENT NUMBER: 125:86967
TITLE: Protein kinase inhibitors for treatment of neurological disorders
INVENTOR(S): Lewis, Michael E.; Kauer, James C.; Neff, Nicola; Glicksman, Marcie; Roberts-Lewis, Jill; Murakata, Chikara; Saito, Hiromitsu; Matsuda, Yuzuru; Kanai, Fumihiko; Kaneko, Masami
PATENT ASSIGNEE(S): Cephalon, Inc., USA; Kyowa Hakko Kogyo Co., Ltd.
SOURCE: PCT Int. Appl., 162 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9613506	A1	19960509	WO 1995-US12965	19951004
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5621100	A	19970415	US 1994-329540	19941026
US 5756494	A	19980526	US 1995-456642	19950602
AU 9539516	A1	19960523	AU 1995-39516	19951004
AU 704314	B2	19990422		
EP 788501	A1	19970813	EP 1995-937391	19951004
EP 788501	B1	20020605		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
BR 9509480	A	19970930	BR 1995-9480	19951004
JP 10510514	T2	19981013	JP 1996-514605	19951004
NZ 295871	A	20010928	NZ 1995-295871	19951004
AT 218571	E	20020615	AT 1995-937391	19951004

PRIORITY APPLN. INFO.:
US 1994-329540 A 19941026
US 1995-456642 A 19950602
US 1992-920102 B2 19920724
US 1993-96561 A2 19930722
WO 1995-US12965 W 19951004
OTHER SOURCE(S): MARPAT 125:86967
GI

L53 ANSWER 29 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



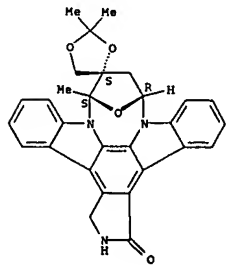
I

AB Staurosporine dimers RNMeCXNHX1NHCXNMeR [R = staurosporine; X = O, S; X1 = alkylene] and K-252a derivs. were prepd. for use as protein kinase inhibitors for treatment of neurol. disorders. Thus, K-252a analog I [R1 =CHO, R2 = Ac] was reduced to I [R = CH2OH] which was treated with EtSH and deacetylated to give I [R1 = CH2SEt, R2 = H, II]. II attenuated the decrease in cholinergic function in the frontal cortex with induced lesions. Choline acetyltransferase in undamaged frontal cortex was unaffected by II.

IT 121664-99-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of K-252a analogs as protein kinase inhibitors)

RN 121664-99-1 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2',3',11',12'-tetrahydro-2,2,9'-trimethyl-, (4S,9'S,12'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L53 ANSWER 29 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

L53 ANSWER 30 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:350578 CAPLUS
DOCUMENT NUMBER: 125:105136
TITLE: K-252 derivatives which enhance neurotrophin-induced activity, and their preparation
INVENTOR(S): Glicksman, Marcie A.; Hudkins, Robert L.; Rotella, David P.; Neff, Nicola T.; Murakata, Chikara
PATENT ASSIGNEE(S): Cephalon, Inc., USA; Kyowa Hakko Kogyo Co., Ltd.
SOURCE: U.S., 21 pp., Cont.-in-part of U.S. 5,468,872. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5516772	A	19960514	US 1994-307530	19940916
US 5468872	A	19951121	US 1993-122893	19930916
CA 2171561	AA	19950323	CA 1994-2171561	19940916
HU 74679	A2	19970128	HU 1996-657	19940916
ES 2160637	T3	20011116	ES 1994-929228	19940916
NZ 314037	A	20000929	NZ 1997-314037	19970108

PRIORITY APPLN. INFO.: US 1993-122893 A2 19930916
OTHER SOURCE(S): MARPAT 125:105136

AB Derivs. of the indolocarbazole alkaloid K-252a are disclosed, which are useful for enhancing neurotrophin-induced activity of neurotrophin responsive cells. A particularly preferred neurotrophin is NT-3, and a particularly preferred neurotrophin responsive cell is one which comprises a trk receptor. The enhanced neurotrophin-induced activity occasioned by the disclosed K-252a derivs. may be detd. by ChAT activity, DRG neuronal survival, or cell division (mitogenesis).

IT **170719-69-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(K-252 derivs.for enhancement of neurotrophin-induced activity, measurement of activity enhancement, and deriv. prepn.)

RN 170719-69-4 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine]-1',3'(2'H)-dione, 2'-amino-11',12'-dihydro-2,2,9'-trimethyl-, [9'S-(9'.alpha.,10'.alpha.,12'.alpha.)]- (9CI) (CA INDEX NAME)

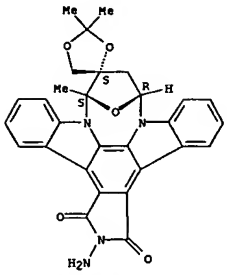
Absolute stereochemistry.

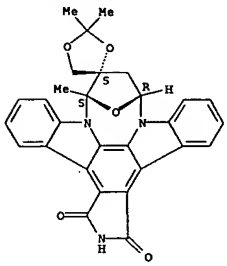
L53 ANSWER 30 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

IT **121679-09-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(K-252 derivs.for enhancement of neurotrophin-induced activity, measurement of activity enhancement, and deriv. prepn.)

RN 121679-09-2 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine]-1',3'(2'H)-dione, 11',12'-dihydro-2,2,9'-trimethyl-, [9'S-(9'.alpha.,10'.beta.,12'.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



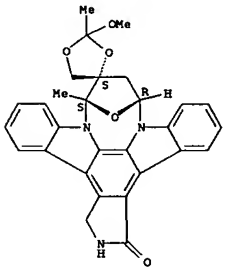


L53 ANSWER 30 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

IT **121665-38-1P 122605-43-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(K-252 derivs.for enhancement of neurotrophin-induced activity, measurement of activity enhancement, and deriv. prepn.)

RN 121665-38-1 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2',3',11',12'-tetrahydro-2-methoxy-2,9'-dimethyl-, (4S,9'S,12'R)- (9CI) (CA INDEX NAME)

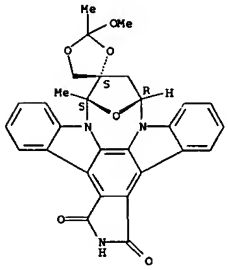
Absolute stereochemistry.



RN 122605-43-0 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine]-1',3'(2'H)-dione, 11',12'-dihydro-2-methoxy-2,9'-dimethyl-, (4S,9'S,12'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

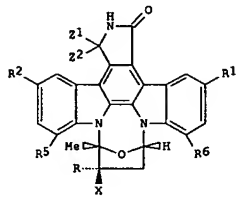
L53 ANSWER 30 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



L53 ANSWER 31 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:350577 CAPLUS
DOCUMENT NUMBER: 125:86695
TITLE: Use of indolocarbazole derivatives to treat a pathological condition of the prostate
INVENTOR(S): Dionne, Craig A.; Contreras, Patricia C.; Murakata, Chikara
PATENT ASSIGNEE(S): Cephalon, Inc., USA; Kyowa Hakko Kogyo Co., Ltd.
SOURCE: U.S., 45 pp., Cont.-in-part of U.S. Ser. No. 96,622, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5516771	A	19960514	US 1994-250175	19940527
CA 2163904	AA	19941208	CA 1994-2163904	19940527
EP 839814	A2	19980506	EP 1998-200023	19940527
EP 839814	A3	19980916		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
AT 165097	E	19980515	AT 1994-918168	19940527
ES 2118414	T3	19980916	ES 1994-918168	19940527
JP 2002356487	A2	20021213	JP 2002-153049	19940527
US 5654427	A	19970805	US 1995-463680	19950605

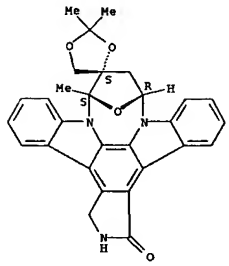
PRIORITY APPLN. INFO.: US 1993-69178 A2 19930528
US 1993-96622 B2 19930722
EP 1994-918168 A3 19940527
JP 1995-501026 A3 19940527
US 1994-250175 A3 19940527
OTHER SOURCE(S): MARPAT 125:86695
GI



I

AB The invention features a method of treating a pathol. condition of the prostate gland, e.g., benign prostatic hypertrophy or prostate cancer, in a mammal, said method comprising administering to said mammal a

L53 ANSWER 31 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



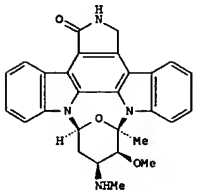
L53 ANSWER 31 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
therapeutic amt. of the indolocarbazole compd. K-252a (I; R = OH, R1 = R2 = R5 = R6 = Z1 = Z2 = H, X = CO2Me) or a preferred deriv. thereof. The invention also includes novel derivs. I of K-252a, wherein Z1 = Z2 = H, R is selected from OH, O-alkyl of 1-6 carbons and O-acyl of 2-6 carbons, X is selected from H, CONHPh (with the proviso that both R1 and R2 are not Br), CH2Y wherein Y is OR7 (wherein R7 is H or acyl of 2-5 carbons, preferably Ac), SOR8 (wherein R8 is alkyl of 1-3 carbons, aryl, or a heterocyclic group including a nitrogen), NR9NR10 (wherein R9 and R10, independently, are H, alkyl of 1-3 carbons, Pro, Ser, Gly, Lys, or acyl), SR16 (wherein R16 ia an aryl, alkyl of 1-3 carbons, or a heterocyclic group including a nitrogen), N3, CO2Me, S-glc, CONR11R12 (wherein R11 and R12, independently, are H, alkyl of 1-6 carbons, Ph, hydroxyalkyl of 1-6 carbons, or R11R12 = CH2CH2OCH2CH2), CO2Me, CH:NNHCONH2, CONHOH, CH:NOH, CH:NNHC(:NH)NH2, CH:NNH-(2-imidazolyl), CH:NN(R17)2 (wherein R17 = aryl), CH2NHCONHR18 (wherein R18 is lower alkyl or aryl); X and R combined form CH2NHCO2, CH2COMe2O, O, CH2NMeCO2. In I, R1, R2, R5, R6 are, independently, H, up to 2 are F, Cl, Br, iodo, No2, CH, OH; NHCONHR13(wherein R13 is Ph or alkyl of 1-3 carbons, with the proviso that only one of R1, R2, R5, R6 is NHCONHR13), CH2OR13 (R13 is alkyl of 1-6 carbons), CH2OCONHR14, NHCOI2R14 (wherein R14 is lower alkyl), CH(SPh)2, CH(SCH2CH2S); R1 = CH2S(O)pR21 (wherein p = 0, 1 and R21 is aryl, alkyl of 1-3 carbons, a heterocyclic group that includes a nitrogen), or R22R23 = (CH2)4, CH2CH2OCH2CH2, CH2CH2NMeCH2CH2, with the proviso that R22 and R23 cannot both be H and at least one of R22 or R23 is H, except when both are alkyl and R2 = R5 = R6 = H; when Z1 and Z2 are comined to represent O, X = CO2Me, R = OH, And R1 = R2 = R5 = R6 = H.

IT 121664-99-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(use of indolocarbazole derivs. to treat a pathol. condition of the prostate)

RN 121664-99-1 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2',3',11',12'-tetrahydro-2,2,9'-trimethyl-, (4S,9'S,12'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L53 ANSWER 32 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:145227 CAPLUS
DOCUMENT NUMBER: 124:202827
TITLE: Staurosporine and ent-Staurosporine: The First Total Syntheses, Prospects for a Regioselective Approach, and Activity Profiles
AUTHOR(S): Link, J. T.; Raghavan, Subharekha; Gallant, Michel; Danishefsky, Samuel J.; Chou, T. C.; Ballas, Lawrence M.
CORPORATE SOURCE: Department of Chemistry, Columbia University, New York, NY, 10027, USA
SOURCE: Journal of the American Chemical Society (1996), 118(12), 2825-42
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

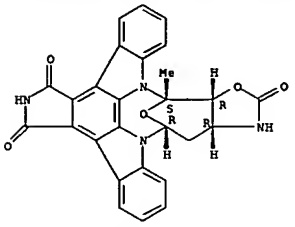
AB The total syntheses of staurosporine and ent-staurosporine I have been achieved. Both glycosidic bonds were built from glycal precursors. The first was constructed by intermol. coupling of an indole anion with a 1,2-anhydro sugar derived from an endo-glycal by direct epoxidn. The second bond was assembled from an exo-glycal by intramol. iodo-glycosidation. Protein kinase C inhibitory activity and cytotoxicity of title compds. are reported.

IT 160256-49-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(total syntheses of staurosporine and ent-staurosporine as protein kinase C inhibitors via regioselective intramol. cyclocondensation of amino sugar)

RN 160256-49-5 CAPLUS
CN 6,11-Epoxy-6H,17H-diindolo[1,2,3-gh:3',2',1'-lm]oxazolo[5,4-c]pyrrolo[3,4-j][1,7]benzodiazonine-8,17,19(6aH,18H)-trione, 9,9a,10,11-tetrahydro-6-methyl-, [6S-(6.alpha.,6a.alpha.,9a.alpha.,11.alpha.)]- (9CI) (CA INDEX NAME)

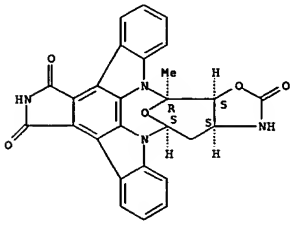
Absolute stereochemistry.

L53 ANSWER 32 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



IT **174291-03-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(total syntheses of staurosporine and ent-staurosporine as protein kinase C inhibitors via regioselective intramol. cyclocondensation of amino sugar)
RN 174291-03-3 CAPLUS
CN 6,11-Epoxy-6H,17H-diindolo[1,2,3-gh:3',2',1'-lm]oxazolo[5,4-c]pyrrolo[3,4-j][1,7]benzodiazonine-8,17,19(6aH,18H)-trione, 9,9a,10,11-tetrahydro-6-methyl-, [6R-(6.alpha.,6a.alpha.,9a.alpha.,11.alpha.)]- (9CI) (CA INDEX NAME)

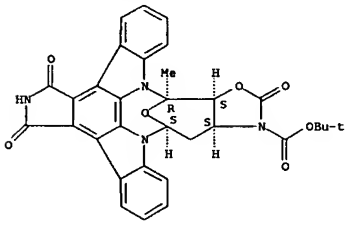
Absolute stereochemistry.



IT **174291-00-0P 174291-01-1P 174291-04-4P**
174291-05-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

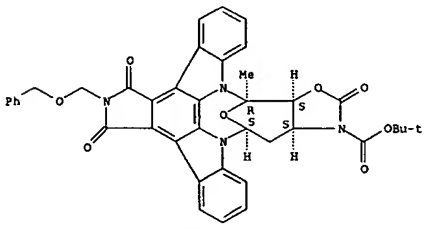
L53 ANSWER 32 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
RN 174291-04-4 CAPLUS
CN 6,11-Epoxy-6H,17H-diindolo[1,2,3-gh:3',2',1'-lm]oxazolo[5,4-c]pyrrolo[3,4-j][1,7]benzodiazonine-9(8H)-carboxylic acid, 6a,9a,10,11,18,19-hexahydro-6-methyl-8,17,19-trioxo-, 1,1-dimethylethyl ester, [6R-(6.alpha.,6a.alpha.,9a.alpha.,11.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 174291-05-5 CAPLUS
CN 6,11-Epoxy-6H,17H-diindolo[1,2,3-gh:3',2',1'-lm]oxazolo[5,4-c]pyrrolo[3,4-j][1,7]benzodiazonine-9(8H)-carboxylic acid, 6a,9a,10,11,18,19-hexahydro-6-methyl-8,17,19-trioxo-18-[(phenylmethoxy)methyl]-, 1,1-dimethylethyl ester, [6R-(6.alpha.,6a.alpha.,9a.alpha.,11.alpha.)]- (9CI) (CA INDEX NAME)

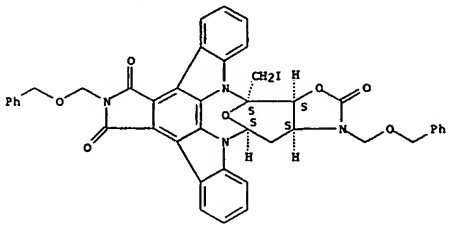
Absolute stereochemistry.



IT **174148-72-2P 174148-73-3P 174291-02-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(total syntheses of staurosporine and ent-staurosporine as protein kinase C inhibitors via regioselective intramol. cyclocondensation of amino sugar)
RN 174148-72-2 CAPLUS

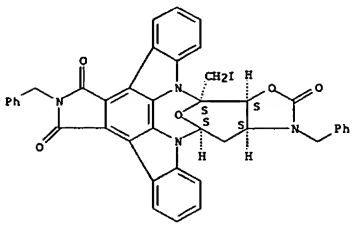
L53 ANSWER 32 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
(total syntheses of staurosporine and ent-staurosporine as protein kinase C inhibitors via regioselective intramol. cyclocondensation of amino sugar)
RN 174291-00-0 CAPLUS
CN 6,11-Epoxy-6H,17H-diindolo[1,2,3-gh:3',2',1'-lm]oxazolo[5,4-c]pyrrolo[3,4-j][1,7]benzodiazonine-8,17,19(6aH,18H)-trione, 9,9a,10,11-tetrahydro-6-(iodomethyl)-9,18-bis[(phenylmethoxy)methyl]-, [6S-(6.alpha.,6a.alpha.,9a.alpha.,11.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



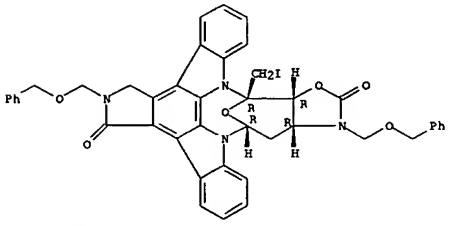
RN 174291-01-1 CAPLUS
CN 6,11-Epoxy-6H,17H-diindolo[1,2,3-gh:3',2',1'-lm]oxazolo[5,4-c]pyrrolo[3,4-j][1,7]benzodiazonine-8,17,19(6aH,18H)-trione, 9,9a,10,11-tetrahydro-6-(iodomethyl)-9,18-bis(phenylmethyl)-, [6S-(6.alpha.,6a.alpha.,9a.alpha.,11.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



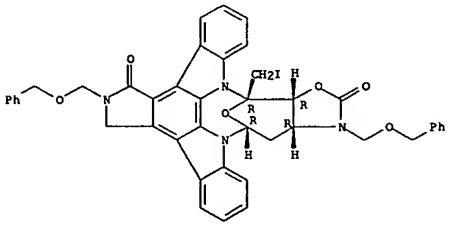
L53 ANSWER 32 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
CN 6,11-Epoxy-6H,17H-diindolo[1,2,3-gh:3',2',1'-lm]oxazolo[5,4-c]pyrrolo[3,4-j][1,7]benzodiazonine-8,17(6aH)-dione, 9,9a,10,11,18,19-hexahydro-6-(iodomethyl)-9,18-bis[(phenylmethoxy)methyl]-, [6R-(6.alpha.,6a.alpha.,9a.alpha.,11.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 174148-73-3 CAPLUS
CN 6,11-Epoxy-6H,19H-diindolo[1,2,3-gh:3',2',1'-lm]oxazolo[5,4-c]pyrrolo[3,4-j][1,7]benzodiazonine-8,19(6aH)-dione, 9,9a,10,11,17,18-hexahydro-6-(iodomethyl)-9,18-bis[(phenylmethoxy)methyl]-, [6R-(6.alpha.,6a.alpha.,9a.alpha.,11.alpha.)]- (9CI) (CA INDEX NAME)

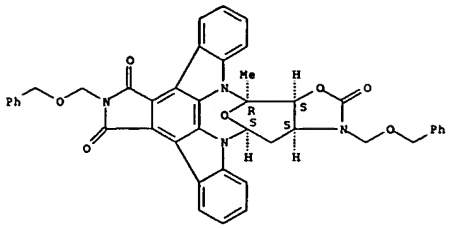
Absolute stereochemistry.



RN 174291-02-2 CAPLUS
CN 6,11-Epoxy-6H,17H-diindolo[1,2,3-gh:3',2',1'-lm]oxazolo[5,4-c]pyrrolo[3,4-j][1,7]benzodiazonine-8,17,19(6aH,18H)-trione, 9,9a,10,11-tetrahydro-6-methyl-9,18-bis[(phenylmethoxy)methyl]-, [6R-(6.alpha.,6a.alpha.,9a.alpha.,11.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L53 ANSWER 32 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



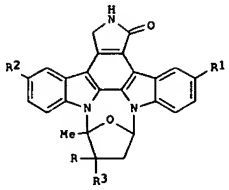
L53 ANSWER 33 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1995:958536 CAPLUS
DOCUMENT NUMBER: 124:202711
TITLE: Preparation of staurosporine derivatives as protein kinase inhibitors for the treatment of neurological disorders
INVENTOR(S): Lewis, Michael E.; Kauer, James C.; Neff, Nicola; Roberts-Lewis, Jill; Murakata, Chikara; Saito, Hiromitsu; Matsuda, Yuzuru; Glicksman, Marcie A.
PATENT ASSIGNEE(S): Cephalon, Inc., USA; Kyowa Hakko Kogyo Co., Ltd.
SOURCE: U.S., 35 pp. Cont.-in-part of U.S. Ser. No. 920,102, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5461146	A	19951024	US 1993-96561	19930722
HU 71239	A2	19951128	HU 1995-192	19930726
EP 768312	A2	19970416	EP 1996-116661	19930726
EP 768312	A3	19970604		
EP 768312	B1	20000906		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
AT 152111	E	19970515	AT 1993-917337	19930726
ES 2101331	T3	19970701	ES 1993-917337	19930726
EP 1002534	A1	20000524	EP 1999-120008	19930726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
AT 196142	E	20000915	AT 1996-116661	19930726
ES 2151629	T3	20010101	ES 1996-116661	19930726
NZ 286198	A	20010629	NZ 1993-286198	19930726
JP 2003113184	A2	20030418	JP 2002-244111	19930726
US 5621100	A	19970415	US 1994-329540	19941026
US 5756494	A	19980526	US 1995-456642	19950602
US 5621101	A	19970415	US 1995-486739	19950607
US 5741808	A	19980421	US 1997-800383	19970214

PRIORITY APPLN. INFO.: US 1992-920102 B2 19920724
US 1993-96561 A2 19930722
EP 1993-917337 A3 19930726
EP 1996-116661 A3 19930726
JP 1994-504731 A3 19930726
US 1994-329540 A2 19941026
US 1995-456642 A3 19950602
OTHER SOURCE(S): MARPAT 124:202711
GI

L53 ANSWER 33 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



I

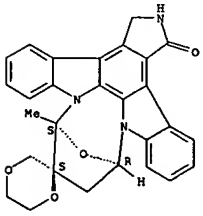
AB The K-252a, and bis-N-substituted derivs. of staurosporine I (R = HO, MeO; R1, R2 = H, Br; R3 = CH2OH, CH2NHCO2Ph, CONHPh, CH2NHCO2Me) were prepd. as protein kinase inhibitors for treatment of diseased neuronal cells. Thus, N-phenylcarbamylstaurosporine was reduced with NaBH4 followed by treatment with carbobenzyloxy-L-serine and hydrogenolysis to give I (R, R1, R2 = H, R3 = CH2NH-Ser). I promoted survival of striatal neurons in the striatal cell survival assay.

IT 173662-34-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of staurosporine derivs. as protein kinase inhibitors for treatment of neurol. disorders)

RN 173662-34-5 CAPLUS

CN Spiro[1,4-dioxane-2,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2',3',11',12'-tetrahydro-9'-methyl-, [9'S-(9'.alpha.,10'.beta.,12'.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L53 ANSWER 34 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1995:931389 CAPLUS
DOCUMENT NUMBER: 124:15478
TITLE: Aqueous indolocarbazole solutions
INVENTOR(S): Goldstein, Joel D.; Herman, Joseph L.
PATENT ASSIGNEE(S): Cephalon, Inc., USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9522331	A1	19950824	WO 1995-US1436	19950203
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9519110	A1	19950904	AU 1995-19110	19950203

PRIORITY APPLN. INFO.: US 1994-199390 19940218
WO 1995-US1436 19950203
OTHER SOURCE(S): MARPAT 124:15478

AB Indolocarbazole solns. are disclosed. The invention features a soln. comprising: (i) an indolocarbazole; (ii) a selected org. solvent being present in a concn. of between about 1% and about 99% by wt. inclusive, (iii) a dispersant being present in a concn. of between about 0.25% and about 10% by wt. inclusive; (i.v.) water being present in a concn. of between 0% and about 99% by wt. inclusive, and (v) a polyethylene glycol being present in a concn. of between 0% and about 60% by wt. inclusive.

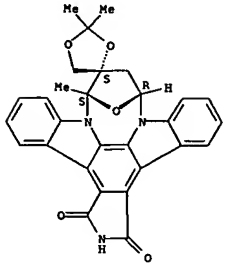
IT 121679-09-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(aq. indolocarbazole pharmaceutical solns.)

RN 121679-09-2 CAPLUS

CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine]-1',3'(2'H)-dione, 11',12'-dihydro-2,2,9'-trimethyl-, [9'S-(9'.alpha.,10'.beta.,12'.alpha.)]- (9CI) (CA INDEX NAME)

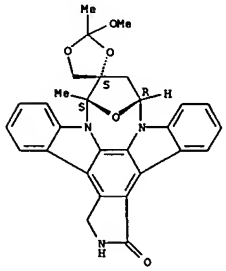
Absolute stereochemistry.

L53 ANSWER 34 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



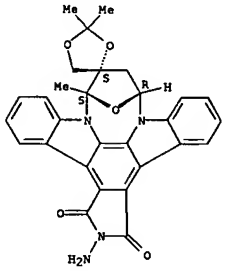
IT 121665-38-1P 122605-43-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(aq. indolocarbazole pharmaceutical solns.)
RN 121665-38-1 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2',3',11',12'-tetrahydro-2-methoxy-2,9'-dimethyl-, (4S,9'S,12'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



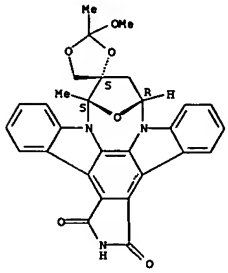
RN 122605-43-0 CAPLUS

L53 ANSWER 34 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



L53 ANSWER 34 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine]-1',3'(2'H)-dione, 11',12'-dihydro-2-methoxy-2,9'-dimethyl-, (4S,9'S,12'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 170719-69-4P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aq. indolocarbazole pharmaceutical solns.)
RN 170719-69-4 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine]-1',3'(2'H)-dione, 2'-amino-11',12'-dihydro-2,2,9'-trimethyl-, [9'S-(9'.alpha.,10'.alpha.,12'.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

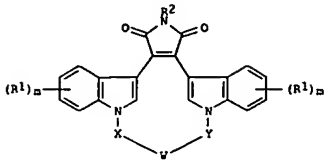
L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:902566 CAPLUS
DOCUMENT NUMBER: 123:314033
TITLE: Preparation of bis(indolyl)maleimide macrocycles as .beta.-isoenzyme selective protein kinase C inhibitors.
INVENTOR(S): Heath, William Francis, Jr.; Jirousek, Michael Robert; Mcdonald, John Hampton, III; Rito, Christopher John
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: Eur. Pat. Appl., 70 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 657458	A1	19950614	EP 1994-308947	19941202
EP 657458	B1	20010822		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2137203	AA	19950608	CA 1994-2137203	19941202
FI 9405706	A	19950608	FI 1994-5706	19941202
NO 9404643	A	19950608	NO 1994-4643	19941202
AU 9479188	A1	19950615	AU 1994-79188	19941202
AU 687909	B2	19980305		
BR 9404831	A	19950808	BR 1994-4831	19941202
JP 07215977	A2	19950815	JP 1994-299399	19941202
CN 1111247	A	19951108	CN 1994-119362	19941202
CN 1050844	B	20000329		
HU 71130	A2	19951128	HU 1994-3468	19941202
HU 219709	B	20010628		
RU 2147304	C1	20000410	RU 1994-42922	19941202
TW 425397	B	20010311	TW 1994-83111226	19941202
AT 204579	E	20010915	AT 1994-308947	19941202
PL 182124	B1	20011130	PL 1994-306084	19941202
ES 2162843	T3	20020116	ES 1994-308947	19941202
CZ 291950	B6	20030618	CZ 1994-3018	19941202
BR 9502611	A	19961001	BR 1995-2611	19950531
US 5698578	A	19971216	US 1996-734292	19961021
CN 1220266	A	19990623	CN 1997-126094	19971209
CN 1055089	B	20000802		
HK 1013827	A1	20020705	HK 1998-115199	19981223
FI 2000000516	A	20000307	FI 2000-516	20000307
FI 2001001109	A	20010528	FI 2001-1109	20010528

PRIORITY APPLN. INFO.: US 1993-163060 A 19931207
US 1994-316973 A 19941003
US 1995-457060 A1 19950601

OTHER SOURCE(S): MARPAT 123:314033
GI

L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



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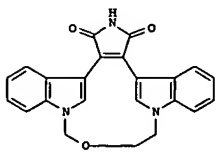

II

AB Title compds. [I; W = O, S, SO, SO2, CO, (substituted) alkylene, alkenylene, arylene, heterocyclylene, CONH, etc.; X, Y = (substituted) alkylene; XYW = (CH2)nA; A = amino acid residue; n = 2-5; R1 = H, halo, alkyl, OH, alkoxy, haloalkyl, NO2, amino, alkylcarbonylamino; R2 = H, Ac, NH2, OH; m = 0-3], were prepd. Thus, 3,4-bis(3'-indolyl)furan-2,5-dione in DMF was treated with NaH and then (BrCH2CH2)2O to give 20% cyclocondensation product, which in DMF was treated with hexamethyldisilazane in MeOH to give 72% title compd. (II). II inhibited protein kinase C .beta.-1 with IC50 = 0.05 .mu.M. I preferentially inhibit the .beta.-isoenzymes by a factor of .gtoreq.10 over other isoenzymes.

IT 169939-85-9P 169939-86-0P 169939-95-1P
169939-96-2P 169939-97-3P 169939-98-4P
169939-99-5P 169940-00-5P 169940-01-6P
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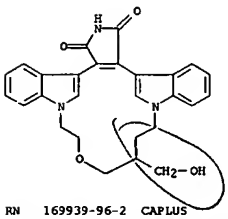
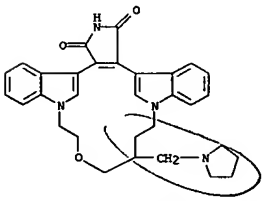
169940-12-9P 169940-13-0P 169940-15-2P
169940-16-3P 169940-17-4P 169940-18-5P
169940-19-6P 169940-20-9P 169940-21-0P
169940-22-1P 169940-23-2P 169940-24-3P
169940-25-4P 169940-26-5P 169940-27-6P
169940-28-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of bis(indolyl)maleimide macrocycles as .beta.-isoenzyme selective protein kinase C inhibitors)

RN 169939-85-9 CAPLUS

L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

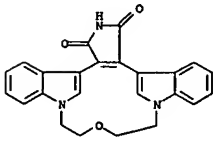


RN 169939-96-2 CAPLUS
CN 5,22:13,18-Dimetheno-19H-dibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacycloheptadecine-19,21(20H)-dione, 6,7,9,10,11,12-hexahydro-10-(1-pyrrolidinylmethyl)- (9CI) (CA INDEX NAME)

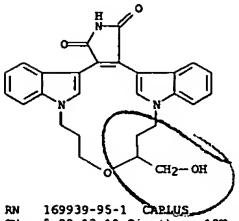


RN 169939-97-3 CAPLUS
CN 5,22:13,18-Dimetheno-19H-dibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacycloheptadecine-19,21(20H)-dione, 10-[(dimethylamino)methyl]-6,7,9,10,11,12-hexahydro-, monohydrochloride (9CI) (CA INDEX NAME)

L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

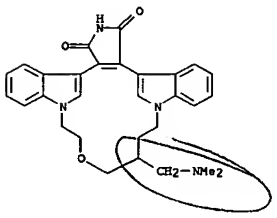


RN 169939-86-0 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecine-19,21(20H)-dione, 7,8,11,12-tetrahydro-8-(hydroxymethyl)- (9CI) (CA INDEX NAME)



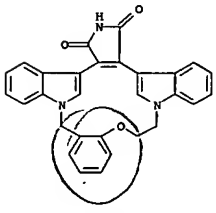
RN 169939-95-1 CAPLUS
CN 5,22:13,18-Dimetheno-19H-dibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacycloheptadecine-19,21(20H)-dione, 6,7,9,10,11,12-hexahydro-10-(hydroxymethyl)- (9CI) (CA INDEX NAME)

L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



● HCl

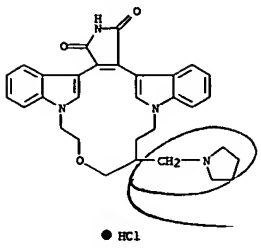
RN 169939-98-4 CAPLUS
CN 1H,17H-9,4:18,23-Dimethenotribenzo[e,k,o]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-1,3(2H)-dione, 10,11-dihydro-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 169939-99-5 CAPLUS
CN 5,22:13,18-Dimetheno-19H-dibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacycloheptadecine-19,21(20H)-dione, 6,7,9,10,11,12-hexahydro-10-(1-pyrrolidinylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

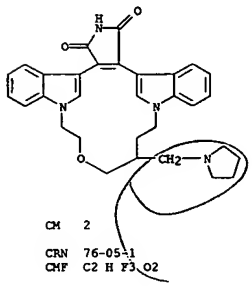


● HCl

RN 169940-00-5 CAPLUS
CN 5,22:13,18-Dimetheno-19H-dibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacycloheptadecine-19,21(20H)-dione, 6,7,9,10,11,12-hexahydro-10-(1-pyrrolidinylmethyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

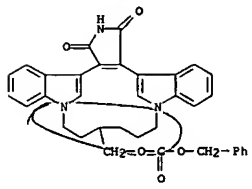
CRN 169939-96-2
CMF C31 H32 N4 O3



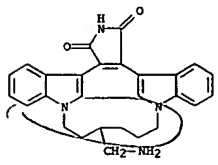
CM 2

CRN 76-05-1
CMF C2 H F3 O2

L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



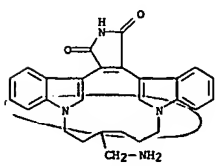
RN 169940-05-0 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-(aminomethyl)-6,7,8,9,10,11-hexahydro- (9CI) (CA INDEX NAME)



RN 169940-06-1 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-(aminomethyl)-6,7,8,9,10,11-hexahydro-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

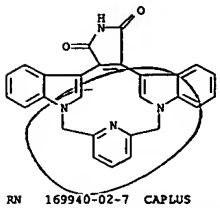
CM 1

CRN 169940-05-0
CMF C27 H26 N4 O2

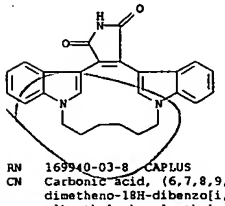


L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

RN 169940-01-6 CAPLUS
CN 6H,12H,19H-5,22:13,18-Dimetheno-7,11-nitrilodibenzo[j,p]pyrrolo[3,4-m][1,9]diazacycloheptadecine-19,21(20H)-dione (9CI) (CA INDEX NAME)



RN 169940-02-7 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro- (9CI) (CA INDEX NAME)



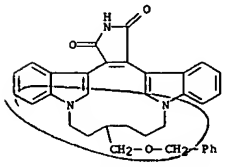
RN 169940-03-8 CAPLUS
CN Carbonic acid, (6,7,8,9,10,11,19,20-octahydro-18,20-dioxo-5,21:12,17-dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecin-8-yl)methyl phenylmethyl ester (9CI) (CA INDEX NAME)

L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

CM 2

CRN 76-05-1
CMF C2 H F3 O2

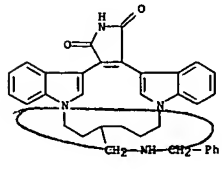
RN 169940-07-2 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-[(phenylmethoxy)methyl]- (9CI) (CA INDEX NAME)



RN 169940-10-7 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-[[(phenylmethyl)amino]methyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 169940-09-4
CMF C34 H32 N4 O2



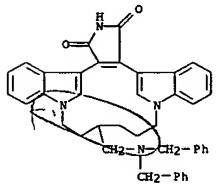
L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 169940-12-9 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-[[bis(phenylmethyl)amino]methyl]-6S,7,8,9,10,11-hexahydro-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 169940-11-8
CMF C41 H38 N4 O2



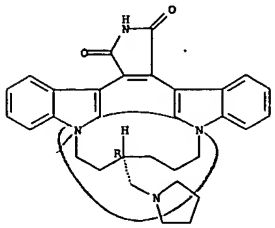
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 169940-13-0 CAPLUS

L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-(1-pyrrolidinylmethyl)-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

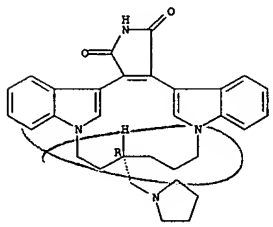
RN 169940-15-2 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-(1-pyrrolidinylmethyl)-, (R)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 169940-14-1
CMF C31 H32 N4 O2

Absolute stereochemistry.

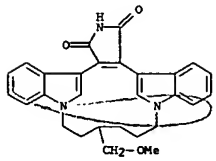
L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



CM 2

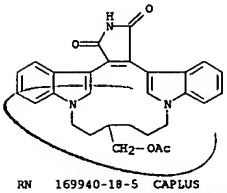
CRN 76-05-1
CMF C2 H F3 O2

RN 169940-16-3 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-(methoxymethyl)- (9CI) (CA INDEX NAME)



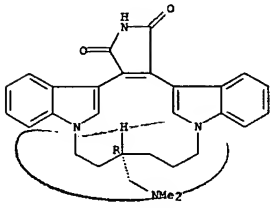
RN 169940-17-4 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-[(acetyloxy)methyl]-6,7,8,9,10,11-hexahydro- (9CI) (CA INDEX NAME)

L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 169940-18-5 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-[(dimethylamino)methyl]-6,7,8,9,10,11-hexahydro-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

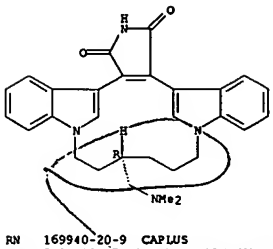


● HCl

RN 169940-19-6 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-[(dimethylamino)methyl]-6,7,8,9,10,11-hexahydro-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

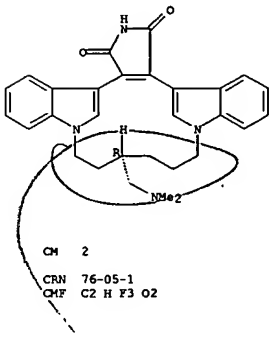


RN 169940-20-9 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-[(dimethylamino)methyl]-6,7,8,9,10,11-hexahydro-, (R)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 169940-19-6
CMF C29 H30 N4 O2

Absolute stereochemistry.



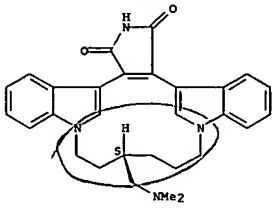
CM 2

CRN 76-05-1
CMF C2 H F3 O2

L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

RN 169940-21-0 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-[(dimethylamino)methyl]-6,7,8,9,10,11-hexahydro-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

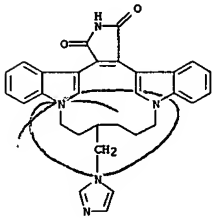
Absolute stereochemistry.



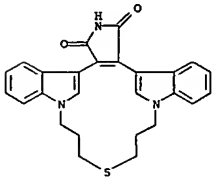
● HCl

RN 169940-22-1 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-(1H-imidazol-1-ylmethyl)- (9CI) (CA INDEX NAME)

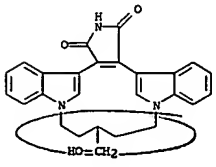
L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 169940-23-2 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]thiadiazacycloheptadecine-19,21(20H)-dione, 7,8,10,11-tetrahydro- (9CI) (CA INDEX NAME)

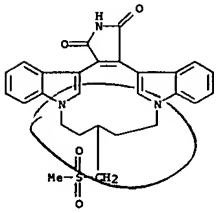


RN 169940-24-3 CAPLUS
CN 6H,17H-5,20:11,16-Dimethenodibenzo[h,n]pyrrolo[3,4-k][1,7]diazacyclopentadecine-17,19(18H)-dione, 7,8,9,10-tetrahydro-8-(hydroxymethyl)- (9CI) (CA INDEX NAME)

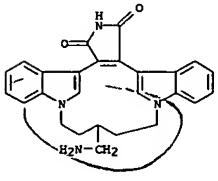


L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

RN 169940-25-4 CAPLUS
CN 6H,17H-5,20:11,16-Dimethenodibenzo[h,n]pyrrolo[3,4-k][1,7]diazacyclopentadecine-17,19(18H)-dione, 7,8,9,10-tetrahydro-8-[(methylsulfonyl)methyl]- (9CI) (CA INDEX NAME)



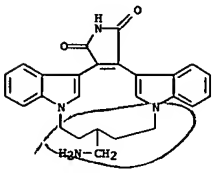
RN 169940-26-5 CAPLUS
CN 6H,17H-5,20:11,16-Dimethenodibenzo[h,n]pyrrolo[3,4-k][1,7]diazacyclopentadecine-17,19(18H)-dione, 8-(aminomethyl)-7,8,9,10-tetrahydro-, monohydrochloride (9CI) (CA INDEX NAME)



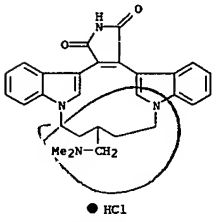
● HCl

RN 169940-27-6 CAPLUS
CN 6H,17H-5,20:11,16-Dimethenodibenzo[h,n]pyrrolo[3,4-k][1,7]diazacyclopentadecine-17,19(18H)-dione, 8-(aminomethyl)-7,8,9,10-tetrahydro- (9CI) (CA INDEX NAME)

L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 169940-28-7 CAPLUS
CN 6H,17H-5,20:11,16-Dimethenodibenzo[h,n]pyrrolo[3,4-k][1,7]diazacyclopentadecine-17,19(18H)-dione, 8-[(dimethylamino)methyl]-7,8,9,10-tetrahydro-, monohydrochloride (9CI) (CA INDEX NAME)

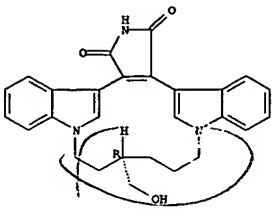


● HCl

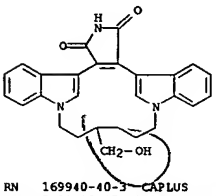
IT 169940-04-9 169940-08-3 169940-40-3
169941-13-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of bis(indolyl)maleimide macrocycles as .beta.-isoenzyme selective protein kinase C inhibitors)
RN 169940-04-9 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-(hydroxymethyl)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

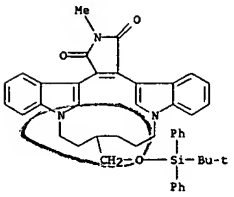


RN 169940-08-3 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-(hydroxymethyl)- (9CI) (CA INDEX NAME)



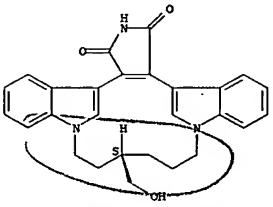
RN 169940-40-3 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-6,7,8,9,10,11-hexahydro-19-methyl- (9CI) (CA INDEX NAME)

L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



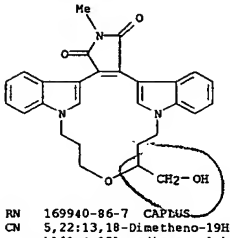
RN 169941-13-3 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-(hydroxymethyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

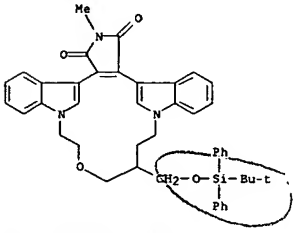


IT 169940-81-2P 169940-86-7P 169940-88-9P
169940-90-3P 169940-94-7P 169940-96-9P
169940-97-0P 169940-98-1P 169941-01-9P
169941-06-4P 169941-10-0P 169941-12-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of bis(indolyl)maleimide macrocycles as .beta.-isoenzyme selective protein kinase C inhibitors)
RN 169940-81-2 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecine-19,21(20H)-dione, 7,8,11,12-tetrahydro-8-(hydroxymethyl)-20-methyl- (9CI) (CA INDEX NAME)

L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

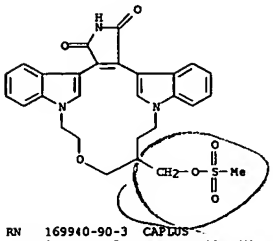


RN 169940-86-7 CAPLUS
CN 5,22:13,18-Dimetheno-19H-dibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacycloheptadecine-19,21(20H)-dione, 10-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-6,7,9,10,11,12-hexahydro-20-methyl- (9CI) (CA INDEX NAME)

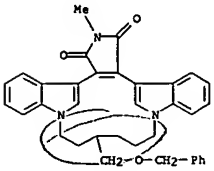


RN 169940-88-9 CAPLUS
CN 5,22:13,18-Dimetheno-19H-dibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacycloheptadecine-19,21(20H)-dione, 6,7,9,10,11,12-hexahydro-10-[[(methylsulfonyl)oxy]methyl]- (9CI) (CA INDEX NAME)

L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

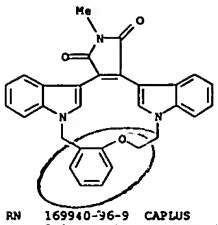


RN 169940-90-3 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-19-methyl-8-[(phenylmethoxy)methyl]- (9CI) (CA INDEX NAME)

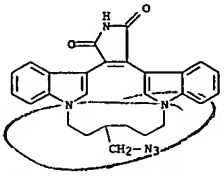


RN 169940-94-7 CAPLUS
CN 1H,17H-9,4:18,23-Dimethenotribenzo[e,k,o]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-1,3(2H)-dione, 10,11-dihydro-2-methyl- (9CI) (CA INDEX NAME)

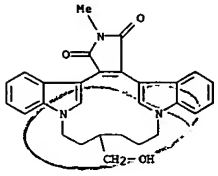
L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 169940-96-9 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 8-(azidomethyl)-6,7,8,9,10,11-hexahydro- (9CI) (CA INDEX NAME)

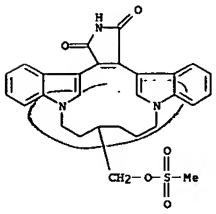


RN 169940-97-0 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-(hydroxymethyl)-19-methyl- (9CI) (CA INDEX NAME)

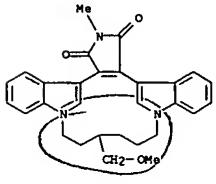


L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

RN 169940-98-1 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-[[(methylsulfonyl)oxy]methyl]- (9CI) (CA INDEX NAME)

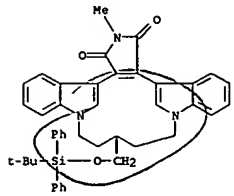


RN 169941-01-9 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-(methoxymethyl)-19-methyl- (9CI) (CA INDEX NAME)

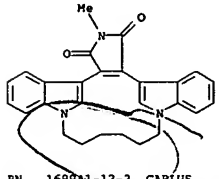


RN 169941-06-4 CAPLUS
CN 6H,17H-5,20:11,16-Dimethenodibenzo[h,n]pyrrolo[3,4-k][1,7]diazacyclopentadecine-17,19(18H)-dione, 8-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-7,8,9,10-tetrahydro-18-methyl- (9CI) (CA INDEX NAME)

L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



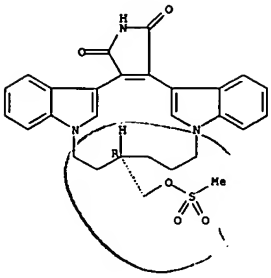
RN 169941-10-0 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-19-methyl- (9CI) (CA INDEX NAME)



RN 169941-12-2 CAPLUS
CN 5,21:12,17-Dimetheno-18H-dibenzo[i,o]pyrrolo[3,4-l][1,8]diazacyclohexadecine-18,20(19H)-dione, 6,7,8,9,10,11-hexahydro-8-[[(methylsulfonyl)oxy]methyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L53 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

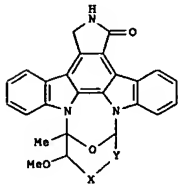


L53 ANSWER 36 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1995:896129 CAPLUS
DOCUMENT NUMBER: 123:314239
TITLE: Preparation of staurosporine derivatives modified in the sugar moiety as selective inhibitors of myosin light chain kinase
INVENTOR(S): Yamada, Rintaro; Seto, Minoru; Sunatsuka, Toshiaki; Oomura, Satoshi
PATENT ASSIGNEE(S): Asahi Chemical Ind, Japan; Kitasato Inst
SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07112987	A2	19950502	JP 1993-280344	19931014

PRIORITY APPLN. INFO.: JP 1993-280344 19931014
OTHER SOURCE(S): MARPAT 123:314239
GI



I

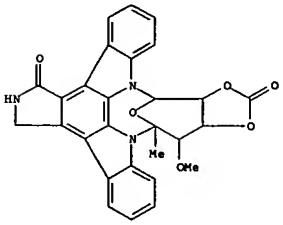
AB The title compds. {I; X = CHR1; Y = CR2R3; or X-Y = CH:CH; wherein R1 = H, OH, C1-4 acyloxy; R2, R3 = H, OH, C1-4 acyloxy, NR4R5; wherein R4, R5 = H or C1-4 acyl; R1R2 or R1R3 = OC(:O)O or OC(:S)O; or R2R3 = :NOH or O; provided that when R1 = H, R2 and R3 are same or different; when R2 and R3 are same, R2R3 = O or :NOH; when R2 and R3 are different, one of R2 and R3 = H and the other = OH, C1-4 acyloxy, or NR4R5; when R1 .noteq. H, (1) one of R2 and R3 = H and the other and R1 are same and represent OH or C1-4 acyloxy or (2) one of R2 and R3 = H and the other and R1 are bonded together to represent OC(:O)O or OC(:S)O}, which have blood platelet aggregation-inhibiting, antitumor, antihypertensive, vasodilatory, and antiinflammatory activities, are prepd. Thus, II [X = CHN(.fwdarw.O)Me2, Y = CH2] (prepn. given) was heated for pyrolysis at 160.degree. and 0.1 mmHg for 5 h to give 85.6% II (X-Y = CH:CH) which was oxidized by OsO4 and 4-methylmorpholine N-oxide in tert-butanol/THF at room temp. for 24 h to

L53 ANSWER 36 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

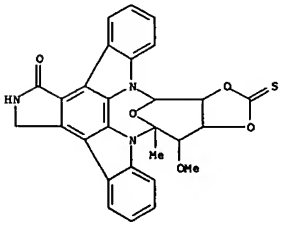
give 65% II (X = Y = CHOH) (III). III showed IC50 of 0.12 and 2.0 .mu.M against protein kinase C and myosin light chain kinase, resp.

IT 169756-24-5P 169756-25-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of staurosporine derivs. modified in sugar moiety as selective inhibitors of myosin light chain kinase)

RN 169756-24-5 CAPLUS
CN 6,11-Epoxy-6H,19H-[1,3]dioxolo[4,5-c]diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonine-8,19-dione, 6a,9a,10,11,17,18-hexahydro-10-methoxy-11-methyl- (9CI) (CA INDEX NAME)

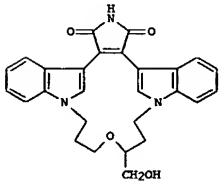


RN 169756-25-6 CAPLUS
CN 6,11-Epoxy-6H,19H-[1,3]dioxolo[4,5-c]diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonin-19-one, 6a,9a,10,11,17,18-hexahydro-10-methoxy-11-methyl-8-thioxo- (9CI) (CA INDEX NAME)



L53 ANSWER 37 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1995:827713 CAPLUS
DOCUMENT NUMBER: 124:29743
TITLE: Synthesis of bisindolylmaleimide macrocycles
AUTHOR(S): Jirousek, Michael R.; Gillig, James R.; Neel, David A.; Rito, Christopher J.; O'Bannon, Douglas; Heath, William F.; McDonald, John H., III; Faul, Margaret M.; Winneroski, Leonard L.
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly Co., Indianapolis, IN, 46285, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1995), 5(18), 2093-6
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 124:29743
GI



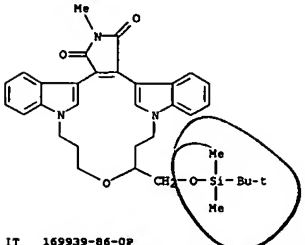
I

AB The synthesis of a novel class of N,N'-macrocyclic bisindolylmaleimides, e.g., I, is reported. The key step involves a remarkably efficient intramol. cyclization reaction. The method was further developed to provide an efficient synthesis of this type of macrocycle through an intermol. alkylation with subsequent intramol. cyclization.

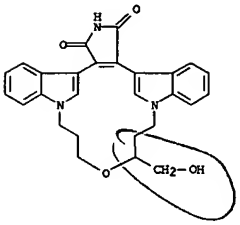
IT 171819-87-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of bisindolylmaleimide macrocycles)

RN 171819-87-7 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecine-19,21(20H)-dione, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-7,8,11,12-tetrahydro-20-methyl- (9CI) (CA INDEX NAME)

L53 ANSWER 37 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



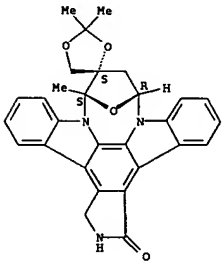
IT 169939-86-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of bisindolylmaleimide macrocycles)
RN 169939-86-0 CAPLUS
CN 10H,19H-5,22:13,18-Dimetheno-6H-dibenzo[f,l]pyrrolo[3,4-i][1,5,14]oxadiazacycloheptadecine-19,21(20H)-dione, 7,8,11,12-tetrahydro-8-(hydroxymethyl)- (9CI) (CA INDEX NAME)



L53 ANSWER 38 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
R1 = R2 = R5 = R6 = Z1 = Z2 = H, X = CONHCH2CH2OH) was prepd. and demonstrated a IC50 of 0.038 .mu.M against the Tsu-Pr1 human prostate cancer cell line.

IT 121664-99-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(claimed compd.; prepn. of indolocarbazole derivs. to treat prostatic cancer and benign prostatic hypertrophy)
RN 121664-99-1 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2',3',11',12'-tetrahydro-2,2,9'-trimethyl-, (4S,9'S,12'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L53 ANSWER 38 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:777654 CAPLUS
DOCUMENT NUMBER: 123:198839
TITLE: Preparation of indolocarbazole derivatives to treat prostatic cancer and hypertrophy
INVENTOR(S): Dionne, Craig A.; Contreras, Patricia C.; Murakata, Chikara
PATENT ASSIGNEE(S): Cephalon, Inc., USA; Kyowa Hakko Kogyo Co., Ltd.
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9427982	A1	19941208	WO 1994-US6082	19940527
W: AU, CA, FI, HU, JP, KR, LK, NO, NZ, PL, RO, RU, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 21639D4	AA	19941208	CA 1994-2163904	19940527
AU 9469607	A1	19941220	AU 1994-69607	19940527
AU 679752	B2	19970710		
EP 699204	A1	19960306	EP 1994-918168	19940527
EP 699204	B1	19980415		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
EP 839814	A2	19980506	EP 1998-200023	19940527
EP 839814	A3	19980916		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
AT 165D97	E	1998D515	AT 1994-918168	19940527
ES 2118414	T3	1998D916	ES 1994-918168	19940527
JP 2002504064	T2	20020205	JP 1995-501026	19940527
JP 3344586	B2	20021111		
JP 2002356487	A2	20021213	JP 2002-153049	19940527
FI 9505709	A	19960103	FI 1995-57D9	19951127
NO 9504816	A	19960126	NO 1995-4816	19951127

PRIORITY APPLN. INFO.: US 1993-69178 A 19930528
US 1993-96622 A 19930722
EP 1994-918168 A3 19940527
JP 1995-501026 A3 19940527
WO 1994-US6082 W 19940527
OTHER SOURCE(S): MARPAT 123:198839
GI

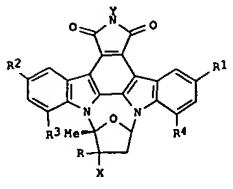
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; R = OH, alkoxy, acyloxy; R1, R2, R5, R6 = H, Cl, F, Br, I, NO2, CN, substituted ureido, etc.; X = H, CONHPh, etc.; Z1, Z2 = H, O (when combined)] [II; R1, R2, R5, R6 = H, halogen, NO2, CN, OH, substituted ureido; R3, R4 = H, alkyl, hydroxyalkyl, alkenyl; Z1, Z2 = H, O (when combined)], useful as inhibitors of tyrosine kinase activity assocd. with neurotropin receptors for treating benign prostatic hypertrophy or prostate cancer, are prepd. Thus, oxadiazepine I (R = OH,

L53 ANSWER 39 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:623503 CAPLUS
DOCUMENT NUMBER: 123:56366
TITLE: K-252a derivatives which enhance neurotrophin-induced activity
INVENTOR(S): Glicksman, Marcie A.; Rotella, David P.; Neff, Nicola; Murakata, Chikara
PATENT ASSIGNEE(S): Cephalon, Inc., USA; Kyowa Hakko Kogyo Co., Ltd.
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 95D7911	A1	1995D323	WO 1994-US10495	19940916
W: AU, CA, FI, HU, JP, KR, NO, NZ, RU, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5468872	A	19951121	US 1993-122893	1993D916
CA 2171561	AA	19950323	CA 1994-2171561	19940916
AU 9478363	A1	19950403	AU 1994-78363	19940916
AU 693480	B2	19980702		
EP 719268	A1	199607D3	EP 1994-929228	19940916
EP 719268	B1	2DD108D1		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
HU 74679	A2	19970128	HU 1996-657	19940916
JP 09502730	T2	19970318	JP 1994-509379	19940916
AT 203751	E	2D010815	AT 1994-929228	19940916
ES 2160637	T3	20011116	ES 1994-929228	19940916
FI 9601236	A	19960315	FI 1996-1236	19960315
NO 9601087	A	19960513	NO 1996-1087	19960315
NZ 314037	A	20000929	NZ 1997-314037	19970108

PRIORITY APPLN. INFO.: US 1993-122893 A 19930916
WO 1994-US10495 W 19940916
OTHER SOURCE(S): MARPAT 123:56366
GI



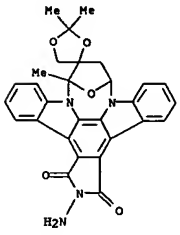
I

AB Indolocarbozole alkaloid K-252a derivs. I (R = OH, OCONH2, alkyl; R1-R4 = H, halo, NO2, cyano, alkyl, amino; Y = H, OH, NH2, alkyl, CHO, OCONH2, benzyl, hydroxyalkyl, aminoalkyl; X = CH2OH, CH2NH2, alkoxymethyl, CO2H, alkoxycarbonyl, substituted carbamoyl; R and X may form a linking group)

L53 ANSWER 39 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
were prepd. as agents useful for enhancing neurotrophin-induced activity of neurotrophin responsive cells. A particularly preferred neurotrophin is NT-3, and a particularly preferred neurotrophin responsive cell is one which coeprises a trk receptor. The enhanced neurotrophin-induced activity occasioned by the disclosed K-252a derivs. may be detd. by the following assays: ChAT activity; DRG neuronal survival; or cell division (mitogenesis).

IT 163968-41-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of K-252a derivs. which enhance neurotrophin-induced activity)

RN 163968-41-0 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine]-1',3'(2'H)-dione, 2'-amino-11',12'-dihydro-2,2,9'-trimethyl- (9CI) (CA INDEX NAME)

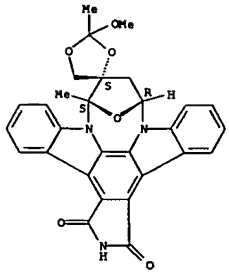


IT 122605-43-0P 163968-46-5P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of K-252a derivs. which enhance neurotrophin-induced activity)

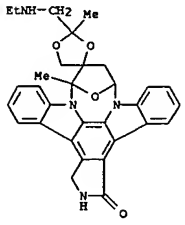
RN 122605-43-0 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine]-1',3'(2'H)-dione, 11',12'-dihydro-2-methoxy-2,9'-dimethyl-, (4S,9'S,12'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L53 ANSWER 39 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



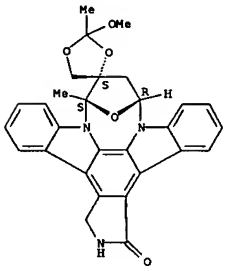
RN 163968-46-5 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2-[(ethylamino)methyl]-2',3',11',12'-tetrahydro-2,9'-dimethyl- (9CI) (CA INDEX NAME)



IT 121665-38-1 121679-09-2 163968-43-2
163968-45-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of K-252a derivs. which enhance neurotrophin-induced activity)

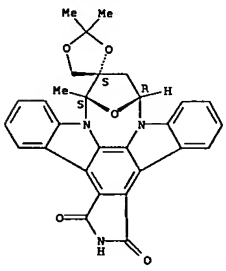
RN 121665-38-1 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2',3',11',12'-tetrahydro-2-methoxy-2,9'-dimethyl-, (4S,9'S,12'R)- (9CI) (CA INDEX NAME)

L53 ANSWER 39 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
Absolute stereochemistry.



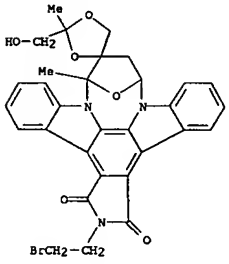
RN 121679-09-2 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine]-1',3'(2'H)-dione, 11',12'-dihydro-2,2,9'-trimethyl-, [9'S-(9'.alpha.,10'.beta.,12'.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



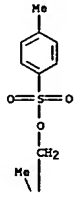
RN 163968-43-2 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine]-1',3'(2'H)-dione, 2'-(2-bromoethyl)-11',12'-dihydro-2-(hydroxymethyl)-2,9'-dimethyl- (9CI) (CA INDEX NAME)

L53 ANSWER 39 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



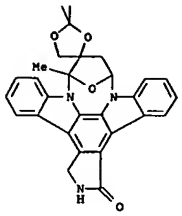
RN 163968-45-4 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2',3',11',12'-tetrahydro-2,9'-dimethyl-2-[[[(4-methylphenyl)sulfonyl]oxy]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



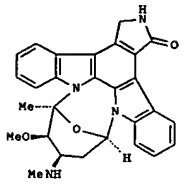
L53 ANSWER 39 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 2-A



L53 ANSWER 40 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1995:283909 CAPLUS
DOCUMENT NUMBER: 122:81720
TITLE: First Total Synthesis of Staurosporine and ent-Staurosporine
AUTHOR(S): Link, J. T.; Raghavan, Subharekha; Danishefsky, Samuel J.
CORPORATE SOURCE: Department of Chemistry, Columbia University, New York, NY, 10027, USA
SOURCE: Journal of the American Chemical Society (1995), 117(1), 552-3
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 122:81720
GI



I

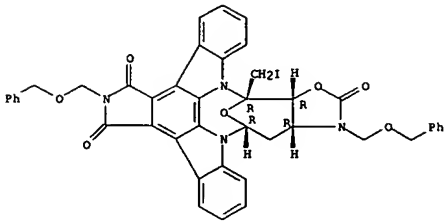
AB The first syntheses of staurosporine (I) and ent-staurosporine are described. The key strategy involved two indole glycosylations guided by an oxazolidinone construct. To promote oxazolidinone ring opening and monomethylation on nitrogen, the oxazolidinone was converted to its N-t-Boc deriv.

IT **160256-47-3P 160256-48-4P 160256-49-5P 160256-50-8P 160256-51-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of staurosporine and ent-staurosporine)

RN 160256-47-3 CAPLUS
CN 6,11-Epoxy-6H,17H-diindolo[1,2,3-gh:3',2',1'-lm]oxazolo[5,4-c]pyrrolo[3,4-j][1,7]benzodiazonine-8,17,19(6aH,18H)-trione, 9,9a,10,11-tetrahydro-6-(iodomethyl)-9,18-bis[(phenylmethoxy)methyl]-, [6R-(6.alpha.,6a.alpha.,9a.alpha.,11.alpha.)]- (9CI) (CA INDEX NAME)

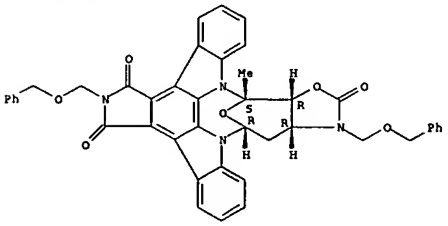
Absolute stereochemistry.

L53 ANSWER 40 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 160256-48-4 CAPLUS
CN 6,11-Epoxy-6H,17H-diindolo[1,2,3-gh:3',2',1'-lm]oxazolo[5,4-c]pyrrolo[3,4-j][1,7]benzodiazonine-8,17,19(6aH,18H)-trione, 9,9a,10,11-tetrahydro-6-methyl-9,18-bis[(phenylmethoxy)methyl]-, [6S-(6.alpha.,6a.alpha.,9a.alpha.,11.alpha.)]- (9CI) (CA INDEX NAME)

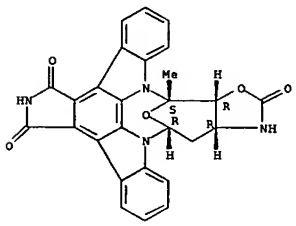
Absolute stereochemistry.



RN 160256-49-5 CAPLUS
CN 6,11-Epoxy-6H,17H-diindolo[1,2,3-gh:3',2',1'-lm]oxazolo[5,4-c]pyrrolo[3,4-j][1,7]benzodiazonine-8,17,19(6aH,18H)-trione, 9,9a,10,11-tetrahydro-6-methyl-, [6S-(6.alpha.,6a.alpha.,9a.alpha.,11.alpha.)]- (9CI) (CA INDEX NAME)

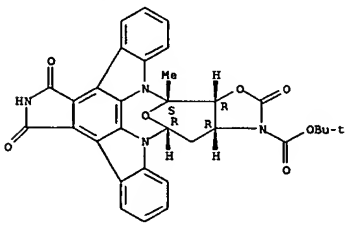
Absolute stereochemistry.

L53 ANSWER 40 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 160256-50-8 CAPLUS
CN 6,11-Epoxy-6H,17H-diindolo[1,2,3-gh:3',2',1'-lm]oxazolo[5,4-c]pyrrolo[3,4-j][1,7]benzodiazonine-9(8H)-carboxylic acid, 6a,9a,10,11,18,19-hexahydro-6-methyl-8,17,19-trioxo-, 1,1-dimethylethyl ester, [6S-(6.alpha.,6a.alpha.,9a.alpha.,11.alpha.)]- (9CI) (CA INDEX NAME)

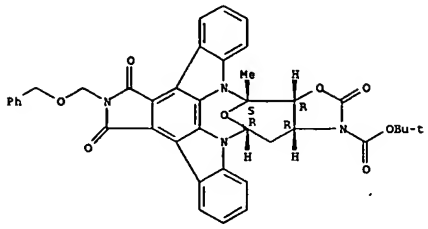
Absolute stereochemistry.



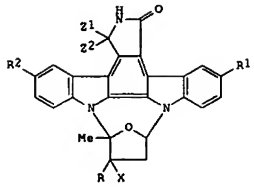
RN 160256-51-9 CAPLUS
CN 6,11-Epoxy-6H,17H-diindolo[1,2,3-gh:3',2',1'-lm]oxazolo[5,4-c]pyrrolo[3,4-j][1,7]benzodiazonine-9(8H)-carboxylic acid, 6a,9a,10,11,18,19-hexahydro-6-methyl-8,17,19-trioxo-18-[(phenylmethoxy)methyl]-, 1,1-dimethylethyl ester, [6S-(6.alpha.,6a.alpha.,9a.alpha.,11.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L53 ANSWER 40 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



L53 ANSWER 41 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



I

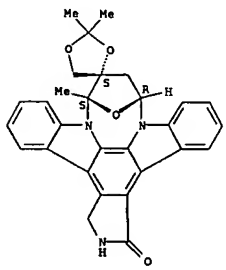
AB QNMeWNMeQ [Q = staurosporine residue; W = C(:Y)NHW'NHC(:Y); W' = C2-20 hydrocarbylene; Y = O, S], K-252a derivs. (I; e.g., R1, R2, Z1, Z2 = H; X = CH2OH; R = OMe), etc., were prepd. Thus, staurosporine was treated with 1,6-hexamethylenebisisocyanate in EtOAc to give 1,6-hexamethylenebis(carbamoylstaurosporine). The latter potentiated the effect of nerve growth factor on stimulation of ornithine decarboxylase activity in PC-12 cells at all concns. tested. K-252a and numerous analogs increased choline acetyltransferase activity in fetal rat spinal cord cultures, promoted dorsal root ganglion neuron survival, etc.

IT 121664-99-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(neuron function enhancing activity of)

RN 121664-99-1 CAPLUS

CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2',3',11',12'-tetrahydro-2,2,9'-trimethyl-, (4S,9'S,12'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L53 ANSWER 41 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1994:680945 CAPLUS
DOCUMENT NUMBER: 121:280945
TITLE: Preparation of bis-staurosporine and K-252a derivatives for enhancing neuron function
INVENTOR(S): Lewis, Michael E.; Neff, Nicola; Roberts-Lewis, Jill; Murakata, Chikara; Saito, Hiromitsu; Matsuda, Yuzuru; Kauer, James C.
PATENT ASSIGNEE(S): Cephalon, Inc., USA; Kyowa Hakko Kogyo Co., Ltd.
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9402488	A1	19940203	WO 1993-US6974	19930726
W: AU, BR, CA, FI, HU, JP, KR, NO, NZ, PT, RU, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 651754	A1	19950510	EP 1993-917337	19930726
EP 651754	B1	19970423		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
HU 71239	A2	19951128	HU 1995-192	19930726
JP 08501080	T2	19960206	JP 1994-504731	19930726
AU 675236	B2	19970130	AU 1993-46881	19930726
AU 9346881	A1	19940214		
EP 768312	A2	19970416	EP 1996-116661	19930726
EP 768312	A3	19970604		
EP 768312	B1	20000906		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
AT 152111	E	19970515	AT 1993-917337	19930726
ES 2101331	T3	19970701	ES 1993-917337	19930726
BR 9306789	A	19981208	BR 1993-6789	19930726
EP 1002534	A1	20000524	EP 1999-120008	19930726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
AT 196142	E	20000915	AT 1996-116661	19930726
ES 2151629	T3	20010101	ES 1996-116661	19930726
NZ 286198	A	20010629	NZ 1993-286198	19930726
JP 2003113184	A2	20030418	JP 2002-244111	19930726
NO 9500242	A	19950307	NO 1995-242	19950123
NO 9900542	A	19990205	NO 1999-542	19950307

PRIORITY APPLN. INFO.: US 1992-920102 A 19920724
EP 1993-917337 A3 19930726
EP 1996-116661 A3 19930726
JP 1994-504731 A3 19930726
WO 1993-US6974 W 19930726

OTHER SOURCE(S): MARPAT 121:280945
GI

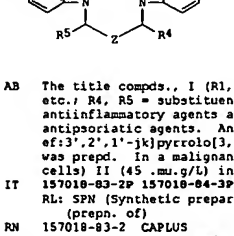
L53 ANSWER 42 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1994:534160 CAPLUS
DOCUMENT NUMBER: 121:134160
TITLE: Diindolo compounds and inflammation inhibitors or neoplasm inhibitors and pharmaceuticals for psoriasis treatment
INVENTOR(S): Vice, Susan F.
PATENT ASSIGNEE(S): Schering Corp., USA
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

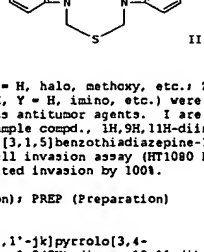
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9407895	A1	19940414	WO 1993-US8276	19930909
W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9351003	A1	19940426	AU 1993-51003	19930909
ZA 9307042	A	19950105	ZA 1993-7042	19930923
CN 1088211	A	19940622	CN 1993-117294	19930924
US 5589472	A	19961231	US 1995-397205	19950310

PRIORITY APPLN. INFO.: US 1992-951052 A2 19920925
WO 1993-US8276 W 19930909

OTHER SOURCE(S): MARPAT 121:134160
GI



I



II

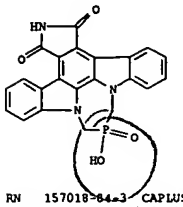
AB The title compds., I (R1, R2 = H, halo, methoxy, etc.; Z = amino, O, S, etc.; R4, R5 = substituent; X, Y = H, imino, etc.) were disclosed. I are antiinflammatory agents and as antitumor agents. I are also useful as antipsoriatic agents. An example compd., 1H,9H,11H-diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione (II) was prepd. In a malignant cell invasion assay (HT1080 human fibrosarcoma cells) II (45 .mu.g/L) inhibited invasion by 100%.

IT 157018-83-2P 157018-84-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

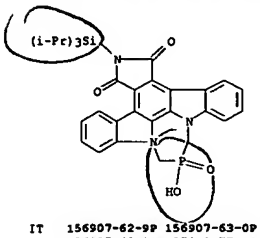
RN 157018-83-2 CAPLUS

CN 1H,9H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][1,5,3]benzodiazaphosphepine-1,3(2H)-dione, 10,11-dihydro-10-hydroxy-, 10-oxide (9CI) (CA INDEX NAME)

L53 ANSWER 42 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

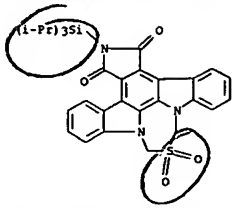


RN 157018-64-3 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][1,5,3]benzodiazaphosphepine-1,3(2H)-dione, 10,11-dihydro-10-hydroxy-2-[tris(1-methylethyl)silyl]-, 10-oxide (9CI) (CA INDEX NAME)



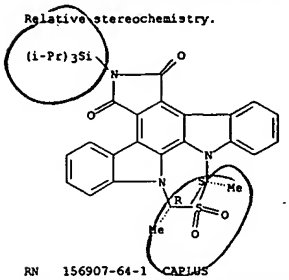
IT 156907-62-9P 156907-63-0P 156907-64-1P
156907-65-2P 157018-77-4P 157018-78-5P
157018-81-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for diindolopyrrolobenzothiadiazepine inflammation inhibitor)
RN 156907-62-9 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 2-[tris(1-methylethyl)silyl]-, 10,10-dioxide (9CI) (CA INDEX NAME)

L53 ANSWER 42 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 156907-63-0 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 9,11-dimethyl-2-[tris(1-methylethyl)silyl]-, 10,10-dioxide, cis- (9CI) (CA INDEX NAME)

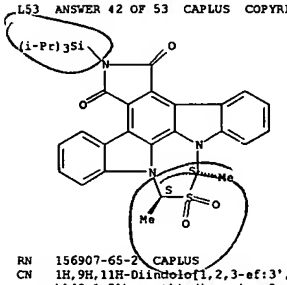
Relative stereochemistry.



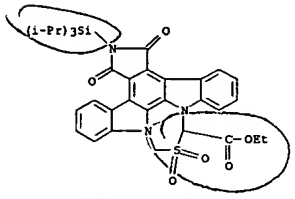
RN 156907-64-1 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 9,11-dimethyl-2-[tris(1-methylethyl)silyl]-, 10,10-dioxide, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

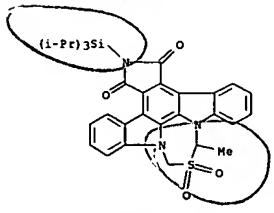
L53 ANSWER 42 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 156907-65-2 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-9-carboxylic acid, 2,3-dihydro-1,3-dioxo-2-[tris(1-methylethyl)silyl]-, ethyl ester, 10,10-dioxide (9CI) (CA INDEX NAME)

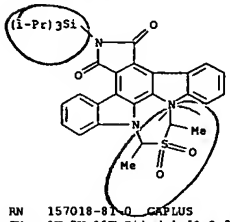


RN 157018-77-4 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 9-methyl-2-[tris(1-methylethyl)silyl]-, 10,10-dioxide (9CI) (CA INDEX NAME)

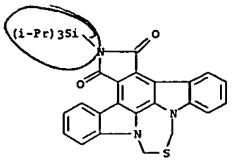


RN 157018-78-5 CAPLUS

L53 ANSWER 42 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 9,11-dimethyl-2-[tris(1-methylethyl)silyl]-, 10,10-dioxide (9CI) (CA INDEX NAME)

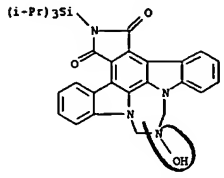


RN 157018-81-0 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 2-[tris(1-methylethyl)silyl]- (9CI) (CA INDEX NAME)

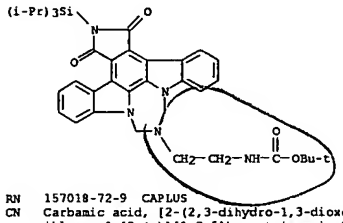


IT 156907-51-6P 157018-71-8P 157018-72-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for diindolopyrrolobenzotriazepinone inflammation inhibitor)
RN 156907-51-6 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',1',2'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepine-1,3(2H)-dione, 10,11-dihydro-10-hydroxy-2-[tris(1-methylethyl)silyl]- (9CI) (CA INDEX NAME)

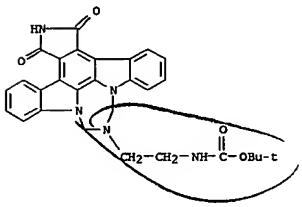
L53 ANSWER 42 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



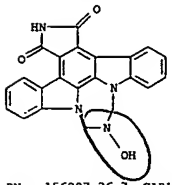
RN 157018-71-8 CAPLUS
CN Carbamic acid, [2-[2,3-dihydro-1,3-dioxo-2-[tris(1-methylethyl)silyl]-1H,9H-diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepin-10(11H)-yl]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



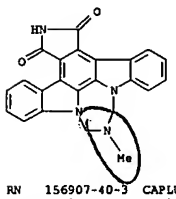
RN 157018-72-9 CAPLUS
CN Carbamic acid, [2-(2,3-dihydro-1,3-dioxo-1H,9H-diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepin-10(11H)-yl)ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



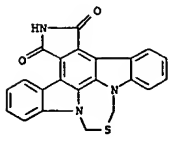
L53 ANSWER 42 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 156907-36-7 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',1',2'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepine-1,3(2H)-dione, 10,11-dihydro-10-methyl- (9CI) (CA INDEX NAME)



RN 156907-40-3 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione (9CI) (CA INDEX NAME)

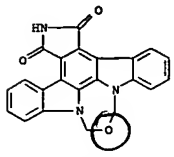


RN 156907-42-5 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepin-1-one, 2,3-dihydro- (9CI) (CA INDEX NAME)

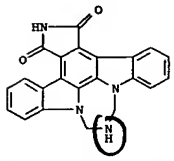
L53 ANSWER 42 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

IT 156907-32-3P 156907-34-5P 156907-35-6P
156907-36-7P 156907-40-3P 156907-42-5P
156907-43-6P 156907-44-7P 156907-45-8P
156907-46-9P 156907-47-0P 156907-48-1P
157018-73-0P 157018-74-1P 157018-79-6P
157018-80-9P 186583-88-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as neoplasm inhibitor or inflammation inhibitor)

RN 156907-32-3 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzoxadiazepine-1,3(2H)-dione (9CI) (CA INDEX NAME)

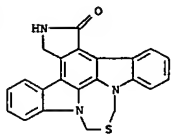


RN 156907-34-5 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',1',2'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepine-1,3(2H)-dione, 10,11-dihydro- (9CI) (CA INDEX NAME)

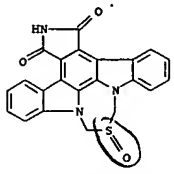


RN 156907-35-6 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',1',2'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepine-1,3(2H)-dione, 10,11-dihydro-10-hydroxy- (9CI) (CA INDEX NAME)

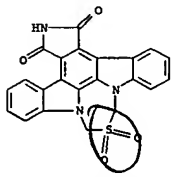
L53 ANSWER 42 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 156907-43-6 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 10-oxide (9CI) (CA INDEX NAME)

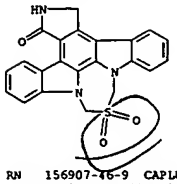


RN 156907-44-7 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 10,10-dioxide (9CI) (CA INDEX NAME)



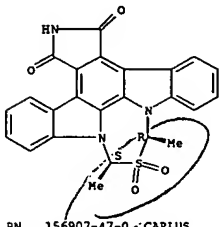
RN 156907-45-8 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepin-1-one, 2,3-dihydro-, 10,10-dioxide (9CI) (CA INDEX NAME)

L53 ANSWER 42 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 156907-46-9 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 9,11-dimethyl-, 10,10-dioxide, cis- (9CI) (CA INDEX NAME)

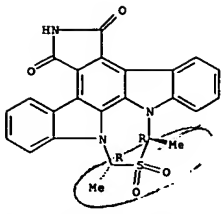
Relative stereochemistry.



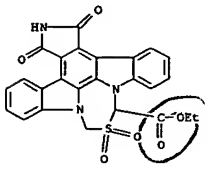
RN 156907-47-0 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 9,11-dimethyl-, 10,10-dioxide, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

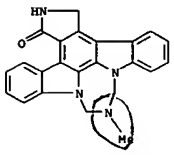
L53 ANSWER 42 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 156907-48-1 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-9-carboxylic acid, 2,3-dihydro-1,3-dioxo-, ethyl ester, 10,10-dioxide (9CI) (CA INDEX NAME)

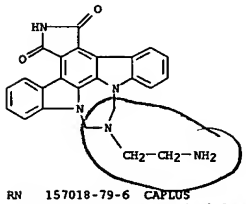


RN 157018-73-0 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepin-1-one, 2,3,10,11-tetrahydro-10-methyl- (9CI) (CA INDEX NAME)

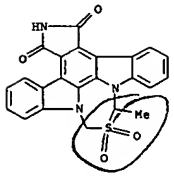


RN 157018-74-1 CAPLUS

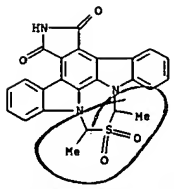
L53 ANSWER 42 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
CN 1H,9H-Diindolo[1,2,3-ef:3',1',2'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepine-1,3(2H)-dione, 10-(2-aminoethyl)-10,11-dihydro- (9CI) (CA INDEX NAME)



RN 157018-79-6 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 9-methyl-, 10,10-dioxide (9CI) (CA INDEX NAME)

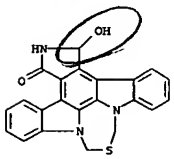


RN 157018-80-9 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 9,11-dimethyl-, 10,10-dioxide (9CI) (CA INDEX NAME)

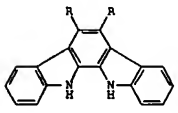


RN 186583-88-0 CAPLUS

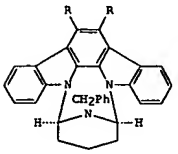
L53 ANSWER 42 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepin-1-one, 2,3-dihydro-3-hydroxy- (9CI) (CA INDEX NAME)



L53 ANSWER 43 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:524570 CAPLUS
DOCUMENT NUMBER: 121:124570
TITLE: Indolocarbazoles. 3. Synthesis of novel aza analogs of staurosporine and K 252a as PKC inhibitors
AUTHOR(S): Shankar, B. B.; Viet, A. Q.; Rizvi, R.; Kirkup, M. P.; McCombie, S. W.; Ganguly, A. K.
CORPORATE SOURCE: Schering-Plough Res. Inst., Kenilworth, NJ, 07033, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1994), 4(3), 495-8
CODEN: BMCLE8; ISSN: 0960-894X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



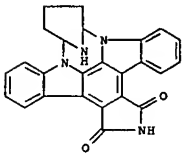
I, R=H
II, RR=CONHCO



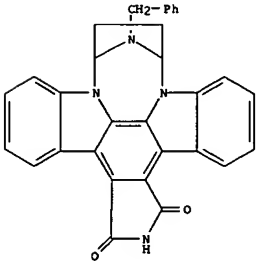
III, R=H
IV, RR=CONHCO

AB Indolocarbazole I and arcyriaflavin A (II) reacted under basic conditions with 1-benzyl-2,6-bis(benzotriazolyl)piperidine to give III and IV. As an extension of this methodol. other related bis benzotriazole derivs. were synthesized and coupled with II to obtain a variety of aza derivs. N-benzylation of these compds. gave novel PKC inhibitors.
IT 155371-66-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and debenzylation of)
RN 155371-66-7 CAPLUS
CN 9,13-Imino-1H,9H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonine-1,3(2H)-dione, 10,11,12,13-tetrahydro-19-(phenylmethyl)- (9CI) (CA INDEX NAME)

L53 ANSWER 43 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

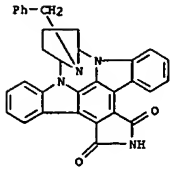


RN 155371-69-0 CAPLUS
CN 9,12-Imino-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-1,3(2H)-dione, 9,10,11,12-tetrahydro-18-(phenylmethyl)- (9CI) (CA INDEX NAME)

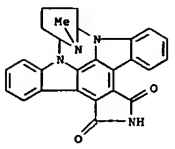


RN 155371-70-3 CAPLUS
CN 9,12-Imino-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-1,3(2H)-dione, 9,10,11,12-tetrahydro-18-methyl- (9CI) (CA INDEX NAME)

L53 ANSWER 43 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

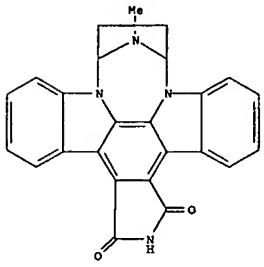


IT 155371-67-8P 155371-68-9P 155371-69-0P
155371-70-3P 155371-71-4P 155371-72-5P
155371-73-6P 155371-74-7P 155371-75-8P
155371-76-9P 155371-77-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and protein kinase C inhibiting activity of)
RN 155371-67-8 CAPLUS
CN 9,13-Imino-1H,9H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonine-1,3(2H)-dione, 10,11,12,13-tetrahydro-19-methyl- (9CI) (CA INDEX NAME)

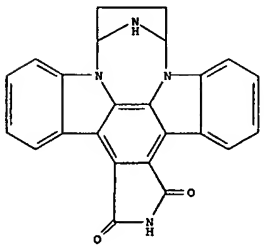


RN 155371-68-9 CAPLUS
CN 9,13-Imino-1H,9H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonine-1,3(2H)-dione, 10,11,12,13-tetrahydro- (9CI) (CA INDEX NAME)

L53 ANSWER 43 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

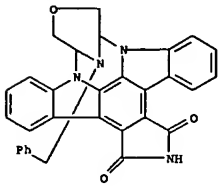


RN 155371-71-4 CAPLUS
CN 9,12-Imino-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-1,3(2H)-dione, 9,10,11,12-tetrahydro- (9CI) (CA INDEX NAME)

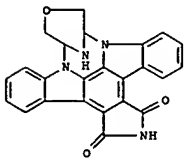


RN 155371-72-5 CAPLUS
CN 9,13-Imino-1H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][4,1,7]benzoxadiazonine-1,3(2H)-dione, 9,10,12,13-tetrahydro-19-(phenylmethyl)- (9CI) (CA INDEX NAME)

L53 ANSWER 43 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

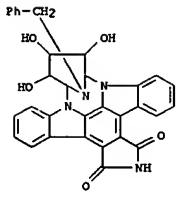


RN 155371-73-6 CAPLUS
CN 9,13-Imino-1H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][4,1,7]benzoxadiazonine-1,3(2H)-dione, 9,10,12,13-tetrahydro- (9CI) (CA INDEX NAME)

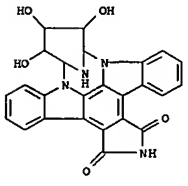


RN 155371-74-7 CAPLUS
CN 9,13-Imino-1H,9H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonine-1,3(2H)-dione, 10,11,12,13-tetrahydro-11,11-bis(methoxymethyl)-19-(phenylmethyl)- (9CI) (CA INDEX NAME)

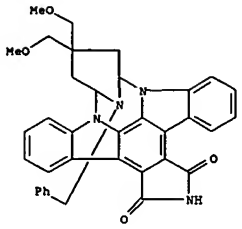
L53 ANSWER 43 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



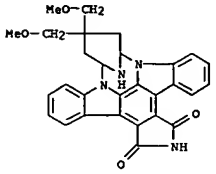
RN 155371-77-0 CAPLUS
CN 9,13-Imino-1H,9H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonine-1,3(2H)-dione, 10,11,12,13-tetrahydro-10,11,12-trihydroxy-, [9R-(9.alpha.,10.beta.,11.alpha.,12.beta.,13.alpha.)]- (9CI) (CA INDEX NAME)



L53 ANSWER 43 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 155371-75-8 CAPLUS
CN 9,13-Imino-1H,9H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonine-1,3(2H)-dione, 10,11,12,13-tetrahydro-11,11-bis(methoxymethyl)- (9CI) (CA INDEX NAME)



RN 155371-76-9 CAPLUS
CN 9,13-Imino-1H,9H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonine-1,3(2H)-dione, 10,11,12,13-tetrahydro-10,11,12-trihydroxy-19-(phenylmethyl)-, [9S-(9.alpha.,10.beta.,11.alpha.,12.beta.,13.alpha.)]- (9CI) (CA INDEX NAME)

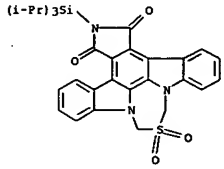
L53 ANSWER 44 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1994:508575 CAPLUS
DOCUMENT NUMBER: 121:108575
TITLE: Indolocarbazole nitrogens linked by three-atom bridges: a potent new class of PKC inhibitors
AUTHOR(S): Vice, Susan F.; Bishop, W. Robert; McCombie, Stuart W.; Dao, Huong; Frank, Emily; Ganguly, Ashit K.
CORPORATE SOURCE: Schering-Plough Res. Inst., Kenilworth, NJ, 07033, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1994), 4(11), 1333-8
CODEN: BMCLE8; ISSN: 0960-894X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two different approaches to prepg. a series of potent PKC inhibitors are delineated, namely, (a) reaction of indolocarbazole derivs. with appropriate 3-atom synthons followed by hydrolysis and/or hydrolysis/redn. or (b) treatment of 2-TIPS Arcyriaflavin A with appropriate 3-atom synthons proceeded by N-Si bond cleavage.

IT 156907-62-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and alkylation of,)

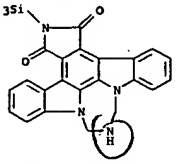
RN 156907-62-9 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 2-[tris(1-methylethyl)silyl]-, 10,10-dioxide (9CI) (CA INDEX NAME)



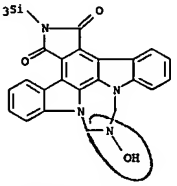
IT 156907-50-5P 156907-51-6P 156907-52-7P
156907-53-8P 156907-54-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and deprotection of)

RN 156907-50-5 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',1',2'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepine-1,3(2H)-dione, 10,11-dihydro-2-[tris(1-methylethyl)silyl]- (9CI) (CA INDEX NAME)

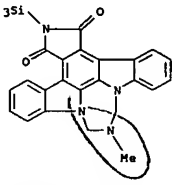
L53 ANSWER 44 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 156907-51-6 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',1',2'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepine-1,3(2H)-dione, 10,11-dihydro-10-hydroxy-2-[tris(1-methylethyl)silyl]- (9CI) (CA INDEX NAME)

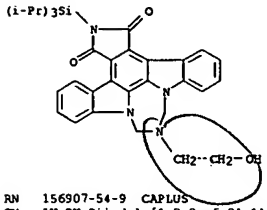


RN 156907-52-7 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',1',2'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepine-1,3(2H)-dione, 10,11-dihydro-10-methyl-2-[tris(1-methylethyl)silyl]- (9CI) (CA INDEX NAME)

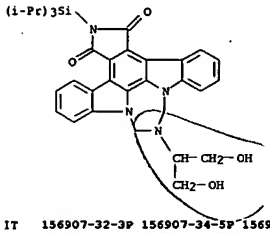


RN 156907-53-8 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',1',2'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepine-

L53 ANSWER 44 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
1,3(2H)-dione, 10,11-dihydro-10-(2-hydroxyethyl)-2-[tris(1-methylethyl)silyl]- (9CI) (CA INDEX NAME)

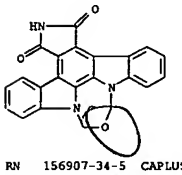


RN 156907-54-9 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',1',2'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepine-1,3(2H)-dione, 10,11-dihydro-10-[2-hydroxy-1-(hydroxymethyl)ethyl]-2-[tris(1-methylethyl)silyl]- (9CI) (CA INDEX NAME)

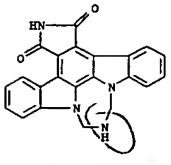


IT 156907-32-3P 156907-34-5P 156907-35-6P
156907-36-7P 156907-37-8P 156907-38-9P
156907-39-0P 156907-40-3P 156907-42-5P
156907-43-6P 156907-44-7P 156907-45-8P
156907-46-9P 156907-47-0P 156907-48-1P
156907-49-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and protein kinase C inhibitory activity of)
RN 156907-32-3 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzoxadiazepine-1,3(2H)-dione (9CI) (CA INDEX NAME)

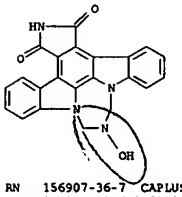
L53 ANSWER 44 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 156907-34-5 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',1',2'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepine-1,3(2H)-dione, 10,11-dihydro- (9CI) (CA INDEX NAME)

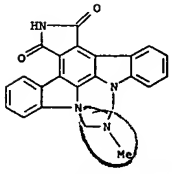


RN 156907-35-6 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',1',2'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepine-1,3(2H)-dione, 10,11-dihydro-10-hydroxy- (9CI) (CA INDEX NAME)

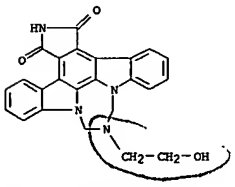


RN 156907-36-7 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',1',2'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepine-1,3(2H)-dione, 10,11-dihydro-10-methyl- (9CI) (CA INDEX NAME)

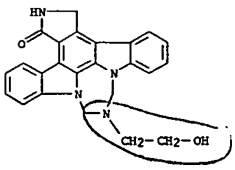
L53 ANSWER 44 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 156907-37-8 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',1',2'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepine-1,3(2H)-dione, 10,11-dihydro-10-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)

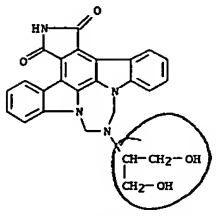


RN 156907-38-9 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepin-1-one, 2,3,10,11-tetrahydro-10-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)

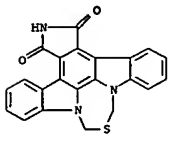


RN 156907-39-0 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',1',2'-jk]pyrrolo[3,4-h][1,3,5]benzotriazepine-1,3(2H)-dione, 10,11-dihydro-10-[2-hydroxy-1-(hydroxymethyl)ethyl]- (9CI) (CA INDEX NAME)

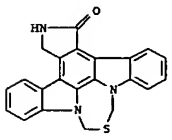
L53 ANSWER 44 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 156907-40-3 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione (9CI) (CA INDEX NAME)



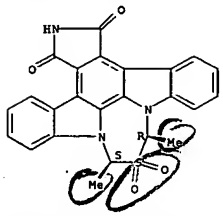
RN 156907-42-5 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepin-1-one, 2,3-dihydro- (9CI) (CA INDEX NAME)



RN 156907-43-6 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 10-oxide (9CI) (CA INDEX NAME)

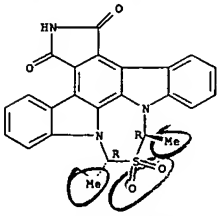
L53 ANSWER 44 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



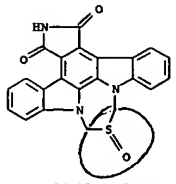
RN 156907-47-0 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 9,11-dimethyl-, 10,10-dioxide, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

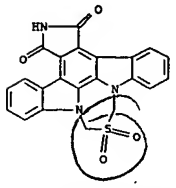


RN 156907-48-1 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-9-carboxylic acid, 2,3-dihydro-1,3-dioxo-, ethyl ester, 10,10-dioxide (9CI) (CA INDEX NAME)

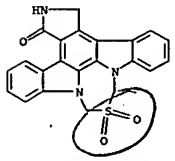
L53 ANSWER 44 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 156907-44-7 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 10,10-dioxide (9CI) (CA INDEX NAME)

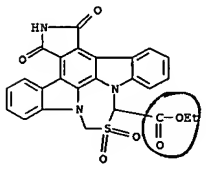


RN 156907-45-8 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepin-1-one, 2,3-dihydro-, 10,10-dioxide (9CI) (CA INDEX NAME)

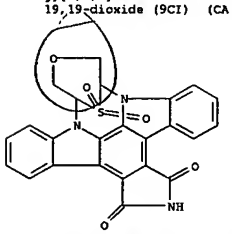


RN 156907-46-9 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 9,11-dimethyl-, 10,10-dioxide,

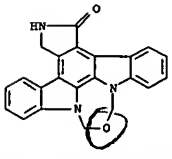
L53 ANSWER 44 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 156907-49-2 CAPLUS
CN 9,13-Epithio-1H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][4,1,7]benzoxadiazonine-1,3(2H)-dione, 9,10,12,13-tetrahydro-, 19,19-dioxide (9CI) (CA INDEX NAME)



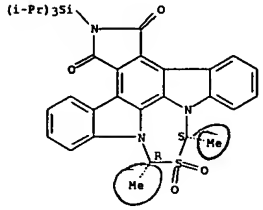
IT 156907-59-4P 156907-63-0P 156907-64-1P
156907-65-2P 156907-66-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 156907-59-4 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzoxadiazepin-1-one, 2,3-dihydro- (9CI) (CA INDEX NAME)



RN 156907-63-0 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-

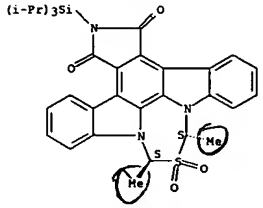
L53 ANSWER 44 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 9,11-dimethyl-2-[tris(1-methylethyl)silyl]-, 10,10-dioxide, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



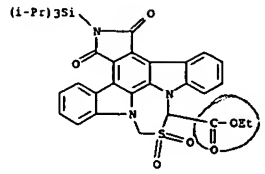
RN 156907-64-1 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-1,3(2H)-dione, 9,11-dimethyl-2-[tris(1-methylethyl)silyl]-, 10,10-dioxide, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

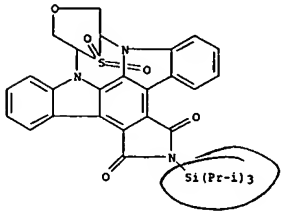


RN 156907-65-2 CAPLUS
CN 1H,9H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][3,1,5]benzothiadiazepine-9-carboxylic acid, 2,3-dihydro-1,3-dioxo-2-[tris(1-methylethyl)silyl]-, ethyl ester, 10,10-dioxide (9CI) (CA INDEX NAME)

L53 ANSWER 44 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



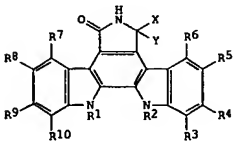
RN 156907-66-3 CAPLUS
CN 9,13-Epithio-1H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][4,1,7]benzoxadiazonine-1,3(2H)-dione, 9,10,12,13-tetrahydro-2-[tris(1-methylethyl)silyl]-, 19,19-dioxide (9CI) (CA INDEX NAME)



L53 ANSWER 45 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:153691 CAPLUS
DOCUMENT NUMBER: 120:153691
TITLE: Use of indolocarbazoles for treatment of AIDS and other disorders
INVENTOR(S): Kleinschroth, Juergen; Hartenstein, Johannes; Schaechtele, Christoph; Rudolph, Claus; Marme, Dieter; Paetzold, Susanne
PATENT ASSIGNEE(S): Goedecke AG, Germany
SOURCE: Ger. Offen., 14 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

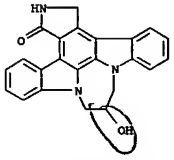
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4217963	A1	19931202	DE 1992-4217963	19920530
WO 9324490	A1	19931209	WO 1993-EP1346	19930528
W: AU, BB, BG, BR, CA, CZ, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9343193	A1	19931230	AU 1993-43193	19930528
PRIORITY APPLN. INFO.:			DE 1992-4217963	19920530
			WO 1993-EP1346	19930528

OTHER SOURCE(S): MARPAT 120:153691
GI

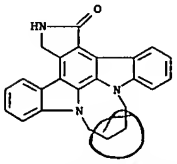


AB The title known compds. (I; R1, R2 = H, alkyl, alkenyl, alkynyl, epoxyalkyl, acyl, aralkyl, cyano, etc., or R1R2 = (substituted) alkylene; R3-R10 = H, alkyl, alkoxy, alkylthio, acyl, halo, NO2, OH, (substituted) amino, etc.; X, Y = H, OH, C1-4 alkoxy, where .gtoreq.1 of X, Y = H) and their salts are useful as immunosuppressants (no data). 12-(2-Cyanoethyl)-6,7,12,13-tetrahydro-5-oxo-5H-indolo[2,3-a]pyrrolo[3,4-c]carbazole was prepd. in improved yield by reaction of 6,7,12,13-tetrahydro-5-oxo-5H-indolo[2,3-a]pyrrolo[3,4-c]carbazole with acrylonitrile and 1,8-diazabicyclo[5.4.0]undec-7-ene at 20.degree. for 15 h, distg. off the solvent under vacuum, taking up the residue in acetone, and filtering out the product.
IT 153206-92-9 153515-97-0
RL: BIOL (Biological study)
(AIDS and other immune disorders and psoriasis treatment with)
RN 153206-92-9 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][1,5]benzodiazepin-1-

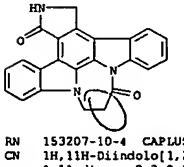
L53 ANSWER 45 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
one, 2,3,10,11-tetrahydro-10-hydroxy- (9CI) (CA INDEX NAME)



RN 153515-97-0 CAPLUS
CN 1H-Diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin-1-one, 2,3,9,10,11,12-hexahydro- (9CI) (CA INDEX NAME)

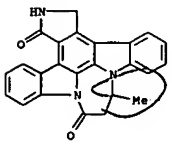


IT 153207-09-1P 153207-10-4P 153207-18-2P
153207-26-2P 153207-91-1P 153207-92-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for AIDS and other immune disorders and psoriasis treatment)
RN 153207-09-1 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][1,5]benzodiazepine-1,9-dione, 2,3,10,11-tetrahydro- (9CI) (CA INDEX NAME)

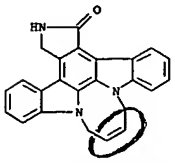


RN 153207-10-4 CAPLUS
CN 1H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][1,5]benzodiazepine-1,11-dione, 2,3,9,10-tetrahydro-9-methyl- (9CI) (CA INDEX NAME)

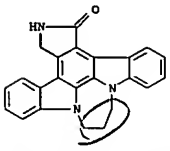
L53 ANSWER 45 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 153207-18-2 CAPLUS
CN 1H-Diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin-1-one, 2,3,9,12-tetrahydro- (9CI) (CA INDEX NAME)

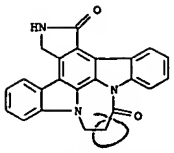


RN 153207-26-2 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][1,5]benzodiazepin-1-one, 2,3,10,11-tetrahydro- (9CI) (CA INDEX NAME)

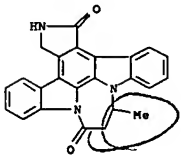


RN 153207-91-1 CAPLUS
CN 1H,11H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][1,5]benzodiazepine-1,11-dione, 2,3,9,10-tetrahydro- (9CI) (CA INDEX NAME)

L53 ANSWER 45 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 153207-92-2 CAPLUS
CN 1H,9H-Diindolo[1,2,3-ef:3',2',1'-jk]pyrrolo[3,4-h][1,5]benzodiazepine-1,9-dione, 2,3,10,11-tetrahydro-11-methyl- (9CI) (CA INDEX NAME)



L53 ANSWER 46 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1994:134148 CAPLUS
DOCUMENT NUMBER: 120:134148
TITLE: Preparation of SF2370 derivatives as protein kinase C inhibitors
INVENTOR(S): Ootsuka, Yasuhisa; Nishimata, Toyoki; Fushihara, Kenichi; Iimori, Takamasa; Ooishi, Takeshi
PATENT ASSIGNEE(S): Meiji Seika Co, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05247054	A2	19930924	JP 1992-45851	19920304
PRIORITY APPLN. INFO.:			JP 1992-45851	19920304

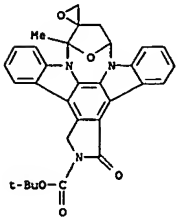
OTHER SOURCE(S): MARPAT 120:134148
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I (R1 = H, Ac, BOC, etc.; C:X = C:O, or C:X represents CHOR; R = H, acyl), useful as protein kinase C inhibitors, were prepd. Title compds. II (R1 = H, Ac, chloroacetyl, etc.; C:X = as above) are also claimed. I and II are also bactericides (no data). Redn. of ketone deriv. III with NaBH4 followed by deprotection gave title compd. IV. IV inhibited protein kinase C with IC50 = 0.42 .mu.g/mL.

IT 153077-29-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as protein kinase C inhibitor)

RN 153077-29-3 CAPLUS
CN Spiro[9,12-epoxy-2H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10(9H)-2'-oxirane]-2-carboxylic acid, 1,3,11,12-tetrahydro-9-methyl-2-oxo-, 1,1-dimethylethyl ester, (9.alpha.,10.beta.,12.alpha.)- (9CI) (CA INDEX NAME)

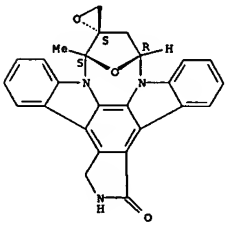


L53 ANSWER 46 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

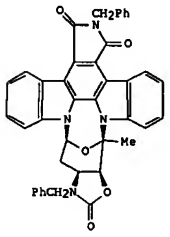
IT 153152-89-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of protein kinase C inhibitor)

RN 153152-89-7 CAPLUS
CN Spiro[9,12-epoxy-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10(9H),2'-oxiran]-1-one, 2,3,11,12-tetrahydro-9-methyl-, (9.alpha.,10.beta.,12.alpha.)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L53 ANSWER 47 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:428486 CAPLUS
DOCUMENT NUMBER: 119:28486
TITLE: The first synthesis of a fully functionalized core structure of staurosporine: sequential indolyl glycosidation by endo and exo glycals
AUTHOR(S): Link, J. T.; Gallant, Michel; Danishefsky, Samuel J.; Huber, Susan
CORPORATE SOURCE: Dep. Chem., Yale Univ., New Haven, CT, 06511-8118, USA
SOURCE: Journal of the American Chemical Society (1993), 115(9), 3782-3
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

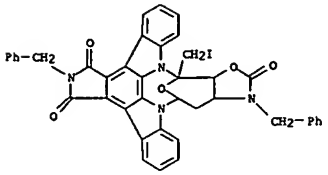
AB The first synthesis of a fully functionalized core structure, i.e. I, of staurosporine is described. The route relies upon a novel intramol. indolyl glycosidation of an exo glycal to give the ring system.

IT 148302-32-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reductive iodination of)

RN 148302-32-3 CAPLUS

CN 6,11-Epoxy-6H,17H-diindolo[1,2,3-gh:3',2',1'-lm]oxazolo[5,4-c]pyrrolo[3,4-j][1,7]benzodiazonine-8,17,19(6aH,18H)-trione, 9,9a,10,11-tetrahydro-6-(iodomethyl)-9,18-bis(phenylmethyl)-, [6R-(6.alpha.,6a.alpha.,9a.alpha.,11.alpha.)]- (9CI) (CA INDEX NAME)

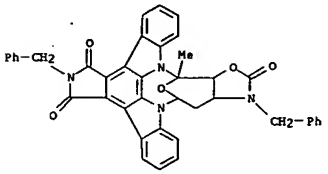
L53 ANSWER 47 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



IT 148302-33-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as functionalized core structure of staurosporine)

RN 148302-33-4 CAPLUS

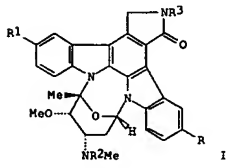
CN 6,11-Epoxy-6H,17H-diindolo[1,2,3-gh:3',2',1'-lm]oxazolo[5,4-c]pyrrolo[3,4-j][1,7]benzodiazonine-8,17,19(6aH,18H)-trione, 9,9a,10,11-tetrahydro-6-methyl-9,18-bis(phenylmethyl)-, (6.alpha.,6a.alpha.,9a.alpha.,11.alpha.)- (9CI) (CA INDEX NAME)



L53 ANSWER 48 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:59419 CAPLUS
DOCUMENT NUMBER: 116:59419
TITLE: Preparation of staurosporinecarboxylic acid derivatives as blood platelet aggregation inhibitors
INVENTOR(S): Yamada, Rintaro; Omura, Satoshi
PATENT ASSIGNEE(S): Asahi Chemical Industry Co., Ltd., Japan; Kitasato Institute
SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 03220194	A2	19910927	JP 1990-329902	19901130
PRIORITY APPLN. INFO.:			JP 1989-308936	19891130

OTHER SOURCE(S): MARPAT 116:59419
GI



I

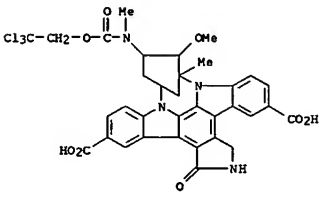
AB The title compds. [I; R,R1 = H, HCO, CO2H, C.ltoreq.5 alkoxycarbonyl; R2 = H, CO2CH2CCl3; R3 = H, acyl] and their salts are prepd. Oxidn. of diformyl compd. I (R = R1 = HCO, R2 = CO2CH2CF3, R3 = Ac) with KMnO4 in 1,4-dioxane, followed by hydrolysis, gave 60% dicarboxy compd. I (R = R1 = CO2H, R2 = CO2CH2CF3, R3 = H), which was reduced with powd. Zn and 2N HCl in Me Cellosolve to give 31% I (R = R1 = CO2H, R2 = R3 = H) (II). II showed the ratio IC50 (platelet aggregation inhibition)/ED50 (vasoconstriction inhibition) = 0.92, vs. 66.0 for staurosporine.

IT 138613-64-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, in prepn. of blood platelet aggregation inhibitor)

RN 138613-64-6 CAPLUS

CN 9,13-Methano-1H,9H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonine-5,17-dicarboxylic acid, 2,3,10,11,12,13-hexahydro-10-methoxy-9-methyl-11-[methyl[(2,2,2-trichloroethoxy)carbonyl]amino]-1-oxo-, [9R-(9.alpha.,10.alpha.,11.alpha.,13.alpha.)]- (9CI) (CA INDEX NAME)

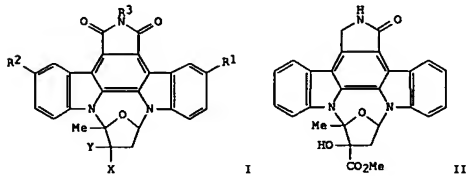
L53 ANSWER 48 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



L53 ANSWER 49 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1989:594456 CAPLUS
DOCUMENT NUMBER: 111:194456
TITLE: Preparation of K-252 derivatives as protein kinase C inhibitors and formulations containing them
INVENTOR(S): Hirata, Tadashi; Mochida, Kenichi; Muragata, Tsutomu; Takahashi, Mitsuru; Kase, Hiroshi; Yamada, Koji; Iwahashi, Kazuyuki; Sato, Akira; Kasai, Masaji; et al.
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 21 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63295589	A2	19881201	JP 1987-327859	19871224
JP 08026037	B4	19960313		
PRIORITY APPLN. INFO.:			JP 1987-12720	19870122

OTHER SOURCE(S): MARPAT 111:194456
GI



I II

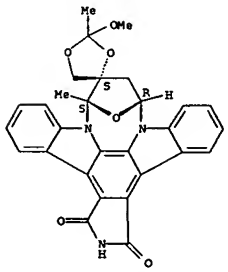
AB The title compds. I [R1,R2 = H, Br, NO2; R3 = H, lower alkyl, aralkyl, etc.; X = CO2H, lower alkoxycarbonyl, carbamoyl, etc.; Y = OH, lower alkoxy, etc.; or YX = OCMe2OCH2, OCSOCH2], useful as protein kinase C inhibitors, were prepd. A mixt. of K-252 (II) and CrO3 in pyridine was stirred at room temp. for 1 day to give K-252 deriv. I (R1 = R2 = R3 = H, X = CO2Me, Y = OH) (III). III in vitro exhibited an IC50 of 0.0069 .mu.g/mL against protein kinase C. A tablet formulation contg. I (R1 = R2 = R3 = H, X = CH2OH, Y = OH) 100, lactose 40, Ca CM-cellulose 10 g, hydroxypropylcellulose and Mg stearate (amt. unspecified) is given.

IT **121664-99-1P 121665-38-1P 122605-43-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, in prepn. of protein kinase C inhibitor)

RN 121664-99-1 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2',3',11',12'-tetrahydro-

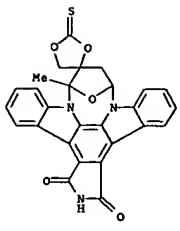
L53 ANSWER 49 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
kl]pyrrolo[3,4-i][1,6]benzodiazocine]-1',3'(2'H)-dione, 11',12'-dihydro-2-methoxy-2,9'-dimethyl-, (4S,9'S,12'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **121665-30-3P 121679-09-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as protein kinase C inhibitor)

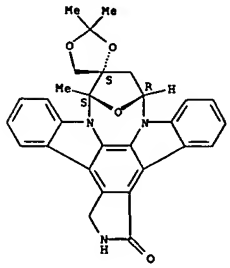
RN 121665-30-3 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine]-1',3'(2'H)-dione, 11',12'-dihydro-9'-methyl-2-thioxo- (9CI) (CA INDEX NAME)



RN 121679-09-2 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine]-1',3'(2'H)-dione, 11',12'-dihydro-2,2,9'-trimethyl-, [9'S-(9'.alpha.,10'.beta.,12'.alpha.)]- (9CI) (CA INDEX NAME)

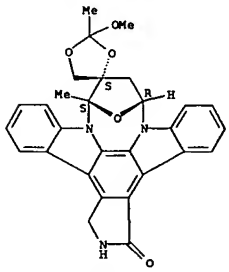
L53 ANSWER 49 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
2,2,9'-trimethyl-, (4S,9'S,12'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 121665-38-1 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2',3',11',12'-tetrahydro-2-methoxy-2,9'-dimethyl-, (4S,9'S,12'R)- (9CI) (CA INDEX NAME)

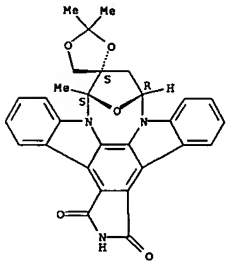
Absolute stereochemistry.



RN 122605-43-0 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-

L53 ANSWER 49 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

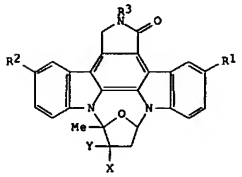
Absolute stereochemistry.



L53 ANSWER 50 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1989:477750 CAPLUS
DOCUMENT NUMBER: 111:77750
TITLE: K-252 derivatives as protein kinase C inhibitors, their preparation, and formulations containing them
INVENTOR(S): Hirata, Tadashi; Mochida, Kenichi; Muragata, Tsutomu; Takahashi, Mitsuru; Kase, Hiroshi; Yamada, Koji; Iwahashi, Kazuyuki; Sato, Akira; Kasai, Masaji; et al.
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 40 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63295588	A2	19881201	JP 1987-327858	19871224
JP 08026036	B4	19960313		
PRIORITY APPLN. INFO.:			JP 1987-12719	19870122

OTHER SOURCE(S): MARPAT 111:77750
GI

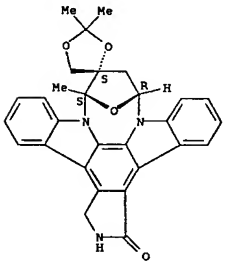


I

AB The title compds. I [R1,R2 = H, Me, hydroxymethyl, lower alkoxymethyl, alkylthiomethyl, etc.; R3 = H, Cl, lower alkanoyl, carbamoyl, etc.; X = hydroxymethyl, CO2H, lower alkoxycarbonyl, etc.; Y = OH, lower alkanoyloxy, etc., or YX = OCMe2OCH2, OCSNHCH2, etc.; provisos are given (for example, when X = hydroxymethyl, CO2H, lower alkoxycarbonyl, at least one of R1-R3 must be other than H)], useful as protein kinase C inhibitors, were prepd. Treatment of I (R1 = NH2, R2 = H, R3 = Ac, X = CO2Me, Y = OAc) (prepn. given) with MeONa, followed by workup and acidification, gave I.HCl (R1 = NH2, R2 = R3 = H, X = CO2Me, Y = OH) (II). II in vitro exhibited an IC50 of 0.175 .mu.g/mL against protein kinase C. A tablet formulation contg. I (R1 = R2 = R3 = H, X = CH:NOH, Y = OH) 100, starch 18, lactose 40, Ca CM-cellulose 10 g, hydroxypropylcellulose, and Mg stearate (amt. unspecified) is given.

IT **111358-94-2P**

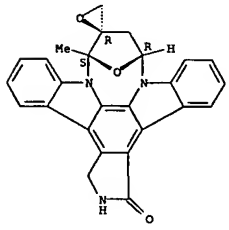
L53 ANSWER 50 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



L53 ANSWER 50 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, in prepn. of protein kinase C inhibitor)

RN 111358-94-2 CAPLUS
CN Spiro[9,12-epoxy-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10(9H),2'-oxiran]-1-one, 2,3,11,12-tetrahydro-9-methyl-, (9S-(9.alpha.,10.alpha.,12.alpha.))- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **121664-99-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as protein kinase C inhibitor)

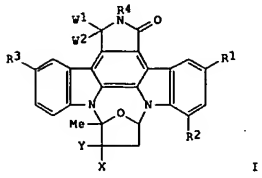
RN 121664-99-1 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2',3',11',12'-tetrahydro-2,2,9'-trimethyl-, (4S,9'S,12'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L53 ANSWER 51 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1989:75861 CAPLUS
DOCUMENT NUMBER: 110:75861
TITLE: Preparation of K-252 derivatives as anticancer agents
INVENTOR(S): Murakata, Chikara; Sato, Akira; Takahashi, Mitsuru; Kobayashi, Eiji; Morimoto, Makoto; Akinaga, Shiro; Hirata, Tadashi; Mochida, Kenichi; Kase, Hiroshi; et al.
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8807045	A1	19880922	WO 1987-JP144	19870309
W: JP, US				
RW: DE, FR, GB				
EP 303697	A1	19890222	EP 1987-901672	19870309
EP 303697	B1	19971001		
R: DE, FR, GB				
US 4923986	A	19900508	US 1988-273519	19881108
PRIORITY APPLN. INFO.:			WO 1987-JP144	19870309

OTHER SOURCE(S): CASREACT 110:75861
GI

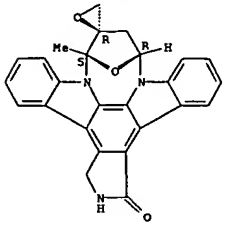


I

AB Title compds. I [R1 = H, Me, OH, HOCH2, alkoxy, Cl, Br, NR5R6 when R3 = H, or R1 = R3 = OH, alkoxy, NH2; R2 = H, NH2; R4 = H, Cl, carbamoyl, alkyl, amino, (CH2)2R7; R5, R6 = alkyl; 1 of R5, R6 = H, carbamoyl, alkylaminocarbonyl and other = H; R7 = Br, NH2, dialkylamino, OH, hydroxyalkylamino; W1, W2 = H or W1W2 = O; X = H, CHO, alkoxycarbonyl, (substituted)aminocarbonyl, substituted Me, CH:NR8; R8 = OH, NH2, guanidino, 2-imidazolylamino; Y = OH, carbamoyloxy; XY = O, CH2O, CH2OCO2, CH2OC(:S)O, CH2NR9CO2 , CH2NHC(S)O, CH2OSO2, CH2N:CR10O; R9 = H, alkyl, aryl, CH2CHO, CH2CH(OH)CH2OH, CH2CH:NNHC(:NH)NH2; R10 = alkyl, alkylthio; several restrictions are stated] are prepd. A soln. of KT5556 (I; R1 - R4 = W1 = W2 = H; X = CO2 H; Y = OH) and Ac2O in pyridine was stirred at room temp. to give 97% I (R1 - R4 = W1 = W2 = H; X = CO2H; Y = OAc), which was treated with SOCl2 to afford 88% I (X = COCl). A soln. of the acid

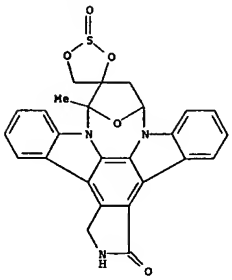
L53 ANSWER 51 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
chloride, HONH2.bul.HCl, and NEt3 in CHCl3 was stirred at room temp. for 6 h, followed by treatment with 1 N NaOH and MeOH, to give 49% I (R1 - R4 = W1 = W2 = H; X = CONHOH; Y = OH), which had IC50 of 0.005, 0.59, and 0.14 .mu.g/mL against protein kinase C, HeLaS3 human cancer cells, and PC-10 human cancer cells, resp.
IT 111358-94-2P 111359-06-9P 111359-07-0P
111359-08-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as anticancer agent)
RN 111358-94-2 CAPLUS
CN Spiro[9,12-epoxy-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10(9H),2'-oxiran]-1-one, 2,3,11,12-tetrahydro-9-methyl-, [9S-(9.alpha.,10.alpha.,12.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

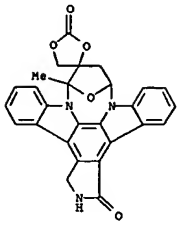


RN 111359-06-9 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine]-1',2-dione, 2',3',11',12'-tetrahydro-9'-methyl-, [9'S-(9'.alpha.,10'.alpha.,12'.alpha.)]- (9CI) (CA INDEX NAME)

L53 ANSWER 51 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

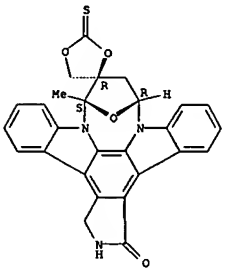


L53 ANSWER 51 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 111359-07-0 CAPLUS
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2',3',11',12'-tetrahydro-9'-methyl-2-thioxo-, [9'S-(9'.alpha.,10'.alpha.,12'.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 111359-08-1 CAPLUS
CN Spiro[1,3,2-dioxathiolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2',3',11',12'-tetrahydro-9'-methyl-, 2-oxide, [9'S-(9'.alpha.,10'.alpha.,12'.alpha.)]- (9CI) (CA INDEX NAME)

L53 ANSWER 52 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1988:221497 CAPLUS
DOCUMENT NUMBER: 108:221497
TITLE: Preparation of SF-2370 derivatives as antihypertensives and diuretics
INVENTOR(S): Koyama, Masao; Hachisu, Mitsugi; Otani, Noriko; Sezaki, Masaji; Kondo, Shinichi
PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 14 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

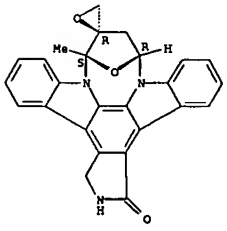
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 62240689	A2	19871021	JP 1986-78249	19860407

PRIORITY APPLN. INFO.: JP 1986-78249 19860407
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. I [X = (dialkyl)amino, (alkyl)amino, PhCH2NH, morpholino, pyrrolidino], useful as antihypertensives and diuretics, are derivs. of SF-2370 (II) and are prepd. from III and IV. Treatment of III with 28% aq. NH3 gave 71% I (X = NH2) (V). At 10 mg/kg orally, V decreased blood pressure in spontaneously hypertensive rats by 11 mm.
IT 111358-94-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, in synthesis of antihypertensive and diuretic)
RN 111358-94-2 CAPLUS
CN Spiro[9,12-epoxy-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10(9H),2'-oxiran]-1-one, 2,3,11,12-tetrahydro-9-methyl-, [9S-(9.alpha.,10.alpha.,12.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



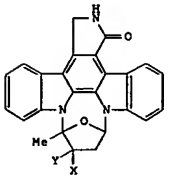
L53 ANSWER 52 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

L53 ANSWER 53 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1987:636751 CAPLUS
DOCUMENT NUMBER: 107:236751
TITLE: Preparation of K-252 derivatives as protein kinase C inhibitors and drugs
INVENTOR(S): Hirata, Tadashi; Takahashi, Mitsuru; Muragata, Tsutomu; Kase, Hiroshi; Yamada, Koji; Iwahashi, Kazuyuki
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 14 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 62155285	A2	19870710	JP 1985-295173	19851227
JP 05001795	B4	19930111		

PRIORITY APPLN. INFO.: JP 1985-295173 19851227
OTHER SOURCE(S): CASREACT 107:236751
GI



I

AB The title compds. [I; X = CR2OH, CH2R1; R = alkyl; R1 = H, OH, N3, guanidino, p-MeC6H4SO3, halo, acyloxy, acylamino, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, (di- or alkyl)amino, morpholino; Y = OH or XY = O, OCH2, CO2CH2, OC(S)OCH2, OCONHCH2, OS(O)OCH2] and their salts, useful as protein kinase C inhibitors and antiinflammatory agents, were prepd. Redn. of K-252 (I; X = CO2Me, Y = OH) with LiAlH4 in THF and reaction of the resulting I (X = CH2OH, Y = OH) with p-MeC6H4SO2Cl in THF contg. Et3N and N,N-dimethylaminopyridine gave I (X = CH2O3SC6H4Me-p, Y = OH) which was treated with NaH in THF to give I (XY = OCH2). A soln. of the latter and morpholine in DMF contg. 1,8-diazabicyclo[5,4,0]-7-undecene was stirred overnight to give I (X = morpholinomethyl, Y = OH). The latter in vitro inhibited protein C kinase with IC50 of 11 ng/mL. I (X = CH2N3, Y = OH) inhibited the release of histamine with IC50 of 3.9 ng/mL

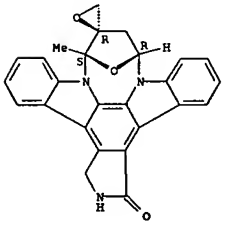
L53 ANSWER 53 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
in rat mast cell medium.

IT 111358-94-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and addn. reaction of, with amines)

RN 111358-94-2 CAPLUS

CN Spiro[9,12-epoxy-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine-10(9H),2'-oxiran]-1-one, 2,3,11,12-tetrahydro-9-methyl-, [9S-(9.alpha.,10.alpha.,12.alpha.)]- (9CI) (CA INDEX NAME)

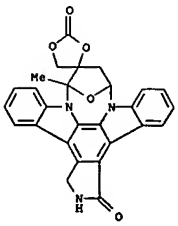
Absolute stereochemistry.



IT 111359-06-9P 111359-07-0P 111359-08-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as inhibitor of protein C kinase, allergy, neoplasms, and inflammation)

RN 111359-06-9 CAPLUS

CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocine]-1',2-dione, 2',3',11',12'-tetrahydro-9'-methyl-, [9'S-(9'.alpha.,10'.alpha.,12'.alpha.)]- (9CI) (CA INDEX NAME)

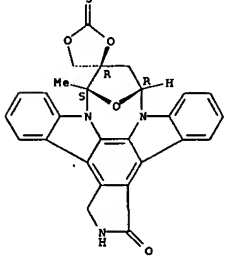


L53 ANSWER 53 OF 53 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

RN 111359-07-0 CAPLUS

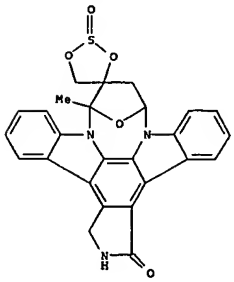
CN Spiro[1,3-dioxolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2',3',11',12'-tetrahydro-9'-methyl-2-thioxo-, [9'S-(9'.alpha.,10'.alpha.,12'.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 111359-08-1 CAPLUS

CN Spiro[1,3,2-dioxathiolane-4,10'(9'H)-[9,12]epoxy[1H]diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin]-1'-one, 2',3',11',12'-tetrahydro-9'-methyl-, 2-oxide, [9'S-(9'.alpha.,10'.alpha.,12'.alpha.)]- (9CI) (CA INDEX NAME)



L54 ANSWER 1 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:570833 CAPLUS
DOCUMENT NUMBER: 139:111682
TITLE: Combined use of a GLP-1 compound and a modulator of diabetic late complications
INVENTOR(S): Knudsen, Lotte Bjerre; Selmer, Johan
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003059372	A2	20030724	WO 2002-DK888	20021220
US 2003144206	A1	20030731	US 2002-328282	20021223

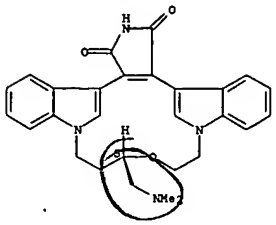
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DK 2001-1969 A 20011229
DK 2002-760 A 20020517
US 2002-350087P P 20020117

AB Methods and uses for treatment of diabetic late complications comprising administration of a GLP-1 compd. and a modulator of diabetic complications.
IT 169939-94-0, Ly 333531
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined use of a GLP-1 compd. and a modulator of diabetic late complications)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 1 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



L54 ANSWER 2 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:460524 CAPLUS
DOCUMENT NUMBER: 139:57624
TITLE: Gray hair-preventive agents and screening method for hair-active ingredients
INVENTOR(S): Kurita, Hiroshi; Nishito, Maki; Shimogaki, Hisao
PATENT ASSIGNEE(S): Lion Corp., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 21 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

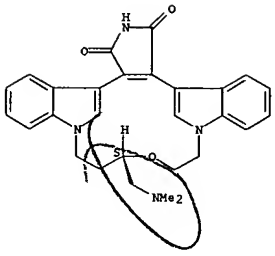
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003171240	A2	20030617	JP 2002-277531	20020924

PRIORITY APPLN. INFO.: JP 2001-298994 A 20010928

AB Gray hair-preventive agents contain .gtoreq.1 substance selected from (a) plants, e.g., Gastrodia elata, Crataegus pinnatifida, Lycii fructus, and Eucommia ulmoides; (b) endothelin receptor agonists; (c) vectors expressing endothelin, stem cell factor (SCF), nerve growth factor (NGF), basic fibroblast growth factor (bFGF), hepatocyte growth factor (HGF), and/or microphthalmia-assocd. transcription factor (MITF); (d) indirubin 3'-oxime, valproate, Li, malantide, kemptide, Ro 32-0432, Ro 31-8220, anisomycin, wortmannin, GF109203X, LY333531, melittin, pseudohypericin, rottlerin; and (e) heparin and heparinoids. The screening method involves bringing test substances into contact with follicular cells or cells near follicles, detg. the amts. of gene expression or protein expression, analyzing the interactions between the test substances and genes, proteins, or other substances, analyzing the actions of the test substances on proliferation of the cells, managing the analyzed results as databases, and detecting or examg. hair-active ingredients based on .gtoreq.2 of the above results. Alternatively, the amts. of melanins per body hair wt. before and after application of test substances to the back of 2- to 12-mo-old, preferably, 4- to 6-mo-old, vitiligo mice (C57BL/6 Mitfmi-vit, C57BL/6 Mivit/vit) are measured for screening of gray hair-preventive ingredients. G. elata ext. (at 100 .mu.g/mL) significantly increased the expression of SCF in human hair papilla cells. The no. of gray hair in men was decreased by application of a compn. contg. 3 wt.% G. elata ext. twice a day for 6 mo.
IT 169939-94-0, LY 333531
RL: BSU (Biological study, unclassified); COS (Cosmetic use); BIOL (Biological study); USES (Uses)
(gray hair-preventive agents and screening method for hair-active ingredients)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

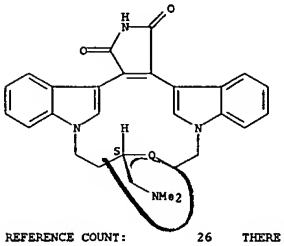
Absolute stereochemistry.

L54 ANSWER 2 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



L54 ANSWER 3 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:267620 CAPLUS
DOCUMENT NUMBER: 139:16988
TITLE: Ruboxistaurin, Eli Lilly
AUTHOR(S): Wheeler, Glen D.
CORPORATE SOURCE: Vancouver, BC, V5Z 1V1, Can.
SOURCE: IDrugs (2003), 6(2), 159-163
CODEN: IDRUFN; ISSN: 1369-7056
PUBLISHER: PharmaPress Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Eli Lilly & Co is developing the protein kinase C-.beta. inhibitor ruboxistaurin, the lead compd. from a series of 14-membered macrocycles, for the potential treatment of diabetic retinopathy, diabetic peripheral neuropathy and macular edema.
IT 169939-94-0P, Ruboxistaurin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmacol. and other properties of protein kinase C-.beta. inhibitor ruboxistaurin)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

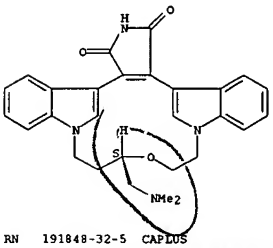


REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 4 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:977372 CAPLUS
DOCUMENT NUMBER: 139:281
TITLE: Disposition of LY333531, a selective protein kinase C .beta. inhibitor, in the Fischer 344 rat and beagle dog
AUTHOR(S): Burkey, J. L.; Campanale, K. M.; O'Bannon, D. D.; Cramer, J. W.; Farid, N. A.
CORPORATE SOURCE: Lilly Research Laboratories, Eli Lilly and Co., Indianapolis, IN, 46285, USA
SOURCE: Xenobiotica (2002), 32(11), 1045-1052
CODEN: XENOBH; ISSN: 0049-8254
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 1. Studies were conducted in the Fischer 344 rat and beagle dog to det. the disposition of LY333531 and its equipotent active desmethyl metabolite, LY338522, both potent and selective inhibitors of the .beta.-isoenzyme of protein kinase C. 2. Male Fischer 344 rats and female beagle dogs received a single 5 mg/kg oral dose of 14C-LY333531. Urine, feces, bile and plasma were collected and analyzed for 14C, LY333531 and LY338522. 3. LY333531 was eliminated primarily in the feces (91 by 120 h in rat, 90 by 96h in dog). Bile contributed the majority of the radioactivity excreted in the feces in rat (66 in the cannulated bile duct study) and a variable but significant proportion in dog. 4. Pharmacokinetics following a single 5 mg/kg oral dose of 14C-LY333531 to the male rat produced Cmax and AUC0-.infin. for LY333531 of 14.7 ng ml-1 and 60.8ng h ml-1, resp., with a half-life of 2.5 h. LY338522 and total radioactivity showed similar profiles. 5. In the female dog at the same dose, Cmax and AUC0-.infin. of LY333531 were higher, producing 245.+-.94 ng ml-1 and 1419.+-.463ng h ml-1, resp., with a half-life of 5.7 h. 6. The data indicate that the disposition of LY333531 is similar in rat and dog.
IT 169939-94-0, LY333531 191848-32-5, LY 338522
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(protein kinase C .beta. inhibitor LY333531 pharmacokinetics and disposition in rats and dogs)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

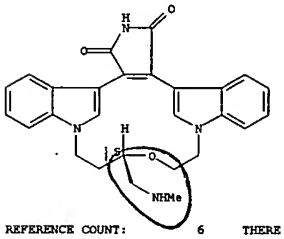
Absolute stereochemistry.

L54 ANSWER 4 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 191848-32-5 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[(methylamino)methyl]-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 5 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:754554 CAPLUS
DOCUMENT NUMBER: 137:257643
TITLE: Methods of modulating angiogenesis
INVENTOR(S): King, George Liang
PATENT ASSIGNEE(S): Joslin Diabetes Center, Inc., USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

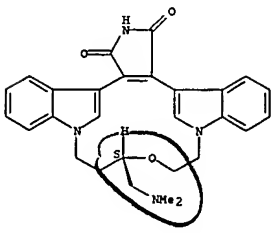
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002077198	A2	20021003	WO 2002-US9509	20020327
WO 2002077198	A3	20021128		
WO 2002077198	C1	20030821		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002165158	A1	20021107	US 2002-107956	20020326

PRIORITY APPLN. INFO.: US 2001-279083P P 20010327
AB Method of modulating angiogenesis in a cell, tissue or subject and methods of treating an angiogenesis-related disorder include modulating PKC activity.
IT 169939-94-0, LY333531
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods of modulating angiogenesis)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

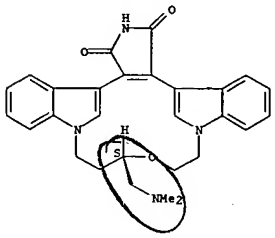
Absolute stereochemistry.



L54 ANSWER 5 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

L54 ANSWER 6 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:730541 CAPLUS
DOCUMENT NUMBER: 138:296866
TITLE: Protein kinase C inhibitors in the treatment and prevention of diabetic complications
AUTHOR(S): Gabriele, Annarita; King, George Liang
CORPORATE SOURCE: Endocrinology Division, Department of Clinical Science, La Sapienza University, Rome, Italy
SOURCE: Current Opinion in Endocrinology & Diabetes (2001), 8(4), 197-204
CODEN: CENDES; ISSN: 1068-3097
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Diabetic complications are known to be assocd. with activation of the protein kinase C pathway through the de novo synthesis of diacylglycerol. Multiple studies have reported that the activation of protein kinase C leads to increased prodn. of extracellular matrix and cytokines and enhances contractility, permeability, and vascular cell proliferation. Specific protein kinase C isoforms, mainly the .beta. and .delta. isoforms, have been shown to be persistently activated in diabetes mellitus. The gene for selective protein kinase C inhibition, LY333531, has been shown to prevent or reverse various vascular dysfunctions in vitro and in vivo. Clin. trials are now ongoing to evaluate the effect of LY333531 on pathol. changes in cardiovascular disease, diabetic retinopathy, neuropathy, and peripheral vascular disease.
IT 169939-94-0, LY333531
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein kinase C inhibitors in treatment and prevention of diabetic complications)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

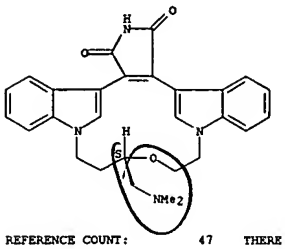


L54 ANSWER 6 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
REFERENCE COUNT: 141 THERE ARE 141 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 7 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:703636 CAPLUS
DOCUMENT NUMBER: 138:335635
TITLE: Effects of the protein kinase C.beta. inhibitor LY333531 on neural and vascular function in rats with streptozotocin-induced diabetes
AUTHOR(S): Cotter, Mary A.; Jack, Alison M.; Cameron, Norman E.
CORPORATE SOURCE: Department of Biomedical Sciences, University of Aberdeen, Foresterhill, Aberdeen, AB25 2ZD, UK
SOURCE: Clinical Science (2002), 103(3), 311-321
CODEN: CSCIAE; ISSN: 0143-5221
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Elevated protein kinase C activity has been linked to the vascular and neural complications of diabetes. The aim of the present study was to examine the involvement of the .beta.-isoform of protein kinase C in abnormalities of neuronal function, neural tissue perfusion and endothelium-dependent vasodilation in diabetes, by treatment with the selective inhibitor LY333531 (10 mg kg-1 day-1). Diabetes was induced in rats by streptozotocin; the duration of diabetes was 8 wk. Nerve conduction velocity was monitored, and responses to noxious mech. and thermal stimuli were estd. by the Randall-Sellito and Hargreaves tests, resp. Sciatic nerve and superior cervical ganglion blood flow were measured by microelectrode polarog. and hydrogen clearance. Vascular responses were examd. using the in vitro mesenteric bed prepn. An 8-wk period of diabetes caused deficits in sciatic motor (20%) and saphenous nerve sensory (16%) conduction velocity, which were reversed by LY333531. Diabetic rats had mech. and thermal hyperalgesia. LY333531 treatment did not affect mech. thresholds, but cor. thermal hyperalgesia. Sciatic nerve and superior cervical ganglion blood flow were both reduced by 50% by diabetes; this was almost completely cor. by 2 wk of LY333531 treatment. Diabetes caused a 32% redn. in vasodilation of the mesenteric vascular bed in response to acetylcholine, mediated by nitric oxide and endothelium-derived hyperpolarizing factor. When the former was abolished during nitric oxide synthase inhibition, an 80% diabetic deficit in the remaining relaxation was noted. LY333531 treatment attenuated the development of these defects by 64% and 53%, resp. Thus protein kinase C.beta. contributes to the neural and vascular complications of exptl. diabetes; LY333531 is a candidate for further study in clin. trials of diabetic neuropathy and vasculopathy.
IT 169939-94-0, LY333531
RL: BUU (Biological use, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of the protein kinase C.beta. inhibitor LY333531 on neural and vascular function in rats with streptozotocin-induced diabetes)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

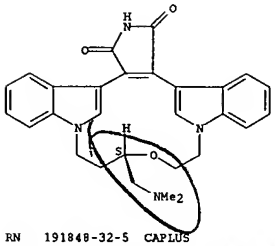
Absolute stereochemistry.

L54 ANSWER 7 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



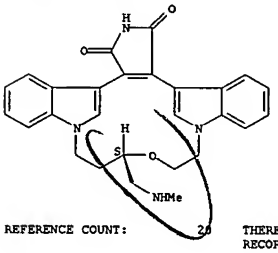
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 8 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 191848-32-5 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[(methylamino)methyl]-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

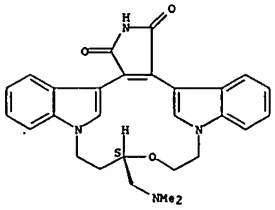
L54 ANSWER 8 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:640281 CAPLUS
DOCUMENT NUMBER: 138:198102
TITLE: The interactions of a selective protein kinase C beta inhibitor with the human cytochromes P450
AUTHOR(S): Ring, Barbara J.; Gillespie, Jennifer S.; Binkley, Shelly N.; Campanale, Kristina M.; Wrighton, Steven A.
CORPORATE SOURCE: Department of Drug Disposition, Lilly Research Laboratories, Eli Lilly and Co., Indianapolis, IN, USA
SOURCE: Drug Metabolism and Disposition (2002), 30(9), 957-961
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Studies were performed to det. the cytochromes P 450 (P 450) responsible for the biotransformation of (S)-13[(dimethylamino)methyl]-10,11,14,15-tetrahydro-4,9:16,21-dimetheno-1H,13H-dibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecene-1,3(2H)-dione (LY333531) to its equipotent metabolite, N-desmethyl LY333531, and to examine the ability of these two compds. to inhibit P 450-mediated metab. Kinetic studies indicated that a single enzyme in human liver microsomes was able to form N-desmethyl LY333531 with an apparent KM value of approx. 1 .mu.M. The formation rate of N-desmethyl LY333531 was correlated with markers of nine P450s in a bank of 20 human liver microsomes. The only significant correlation obsd. was with the form-selective activity for CYP3A. Of the nine cDNA-expressed P450s examd., only CYP3A4 and CYP2D6 formed N-desmethyl LY333531. However, CYP3A4 formed N-desmethyl LY333531 at a rate 57-fold greater than that obsd. with CYP2D6. In incubations with human liver microsomes, quinidine, an inhibitor of CYP2D6, demonstrated little inhibition of metabolite formation while ketoconazole, an inhibitor of CYP3A, demonstrated almost complete inhibition. Thus, CYP3A is responsible for the formation of N-desmethyl LY333531. LY333531 and N-desmethyl LY333531 were also examd. for their ability to inhibit metab. mediated by CYP2D6, CYP2C9, CYP3A, and CYP1A2. LY333531 and N-desmethyl LY333531 were found to competitively inhibit CYP2D6 with calcd. Ki values of 0.17 and 1.0 .mu.M, resp. Less potent inhibition by these compds. of metab. mediated by the other three P450s examd. was obsd. In conclusion, CYP3A is primarily responsible for forming N-desmethyl LY333531. Therefore, alterations in the activity of this enzyme have the potential to affect LY333531 clearance. In addn., LY333531 and its metabolite are predicted to be potential inhibitors of CYP2D6-mediated reactions in vivo.
IT 169939-94-0, LY333531 191848-32-5, N-Desmethyl LY333531
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(interactions of a selective protein kinase C beta inhibitor with the human cytochromes P 450)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 9 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:198513 CAPLUS
DOCUMENT NUMBER: 137:33446
TITLE: Hetero Diels-Alder-Biocatalysis Approach for the Synthesis of (S)-3-[2-((Methylsulfonyl)oxy)ethoxy]-4-(triphenylmethoxy)-1-butanol Sulfonate, a Key Intermediate for the Synthesis of the PKC Inhibitor LY333531
AUTHOR(S): Caille, Jean-Claude; Govindan, C. K.; Junga, Heiko; Lalonde, Jim; Yao, Yiming
CORPORATE SOURCE: PPG-SIPSY, Avrille, 49242, Fr.
SOURCE: Organic Process Research & Development (2002), 6(4), 471-476
CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:33446
AB A cost-effective and easily scaled-up process has been developed for the synthesis of (S)-3-[2-[(methylsulfonyl)oxy]ethoxy]-4-(triphenylmethoxy)-1-butanol sulfonate, a key intermediate used in the synthesis of a protein kinase C inhibitor drug, through a combination of hetero Diels-Alder and biocatalytic reactions. The Diels-Alder reaction between Et glyoxylate and butadiene was used to make racemic 2-ethoxycarbonyl-3,6-dihydro-2H-pyran. Treatment of the racemic ester with Bacillus lentus protease resulted in the selective hydrolysis of the R-enantiomer and yielded S-2-ethoxycarbonyl-3,6-dhydro-2H-pyran in excellent optical purity, which was reduced to S-3,6-dihydro-2H-pyran-2-yl methanol. Tritylation of this alc., followed by reductive ozonolysis and mesylation afforded the product in 10-15% overall yield and with >99% ee and chem. purity. Details of the process development work done on each step are given.
IT 169939-94-0P, LY 333531
RL: PNU (Preparation, unclassified); PREP (Preparation)
(hetero Diels-Alder-biocatalysis approach for the com. synthesis of (S)-3-[2-[(methylsulfonyl)oxy]ethoxy]-4-(triphenylmethoxy)-1-butanol sulfonate, a key intermediate for the synthesis of the PKC inhibitor LY 333531)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 9 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 10 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 10 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:174782 CAPLUS
DOCUMENT NUMBER: 137:370029
TITLE: Anomalous events occurring during the preparation of stable labeled isotopomers
AUTHOR(S): Wheeler, William J.; Douglas, DeLise M.; O'Bannon, Douglas D.; Barbuch, Robert J.; Stoddard, Eli A.
CORPORATE SOURCE: Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, IN, 46285, USA
SOURCE: Synthesis and Applications of Isotopically Labelled Compounds, Proceedings of the International Symposium, 7th, Dresden, Germany, June 18-22, 2000 (2001), Meeting Date 2000, 240-243. Editor(s): Pleiss, Ulrich; Voges, Rolf. John Wiley & Sons Ltd.: Chichester, UK.
CODEN: 69CIJC; ISBN: 0-471-49501-8
DOCUMENT TYPE: Conference
LANGUAGE: English

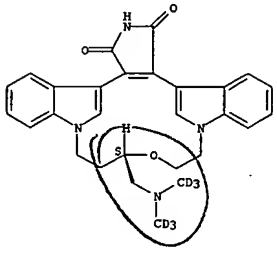
AB The potential pitfalls that may occur in the prepn. of isotopically labeled compds. contg. arom. thioethers and esters, and the problems that may occur when using DMF as a solvent are described. Such labeled isotopomers include thiometine-[N-13CD3], isotopically labeled xanomaline metabolites, and LY333531-[2H6] mesylate. In two cases, these pitfalls were easily avoided by changing the sequence of reactions or by substituting the readily available DMF-d7 as a solvent. In the third case, it was required to design an alternative route for the prepn. of the labeled compd.

IT **475478-39-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(anomalous events occurring during the prepn. of stable labeled isotopomers)

RN 475478-39-8 CAPLUS

CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[[di(methyl-d3)amino]methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L54 ANSWER 11 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:142493 CAPLUS
DOCUMENT NUMBER: 136:194255
TITLE: Treatment of the insulin resistance syndrome
INVENTOR(S): Fryburg, David Albert; Gibbs, Earl Michael; Koppiker, Nandan Parmanand
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

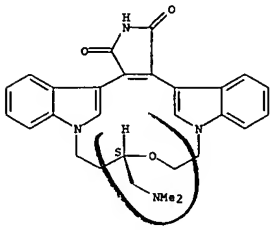
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002013798	A2	20020221	WO 2001-IB1428	20010806
WO 2002013798	A3	20030123		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001076607	A5	20020225	AU 2001-76607	20010806
EP 1307183	A2	20030507	EP 2001-954266	20010806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2002165237	A1	20021107	US 2001-927525	20010810
WO 2002060422	A2	20020808	WO 2002-IB315	20020130
WO 2002060422	A3	20021010		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002143015	A1	20021003	US 2002-60788	20020130
US 2003166662	A1	20030904	US 2003-368826	20030219

PRIORITY APPLN. INFO.:
US 2000-224928P P 20000811
GB 2000-30649 A 20001215
US 2001-266083P P 20010202
GB 2001-6465 A 20010315
GB 2001-6468 A 20010315
GB 2001-17134 A 20010713
US 2000-256431P P 20001218
US 2001-292506P P 20010521
WO 2001-IB1428 W 20010806
US 2001-927525 B1 20010810

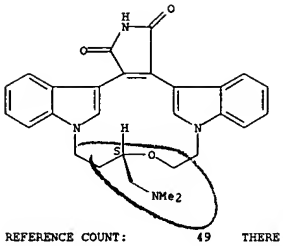
AB Use of a selective cGMP PDE5 inhibitor or a pharmaceutical compn. thereof in the prepn. of a medicament for the curative, palliative or prophylactic treatment of the insulin resistance syndrome wherein the insulin resistance syndrome means the concomitant existence in a subject of two or

L54 ANSWER 11 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
more of: dyslipidemia; hypertension; type 2 diabetes mellitus, impaired glucose tolerance (IGT) or a family history of diabetes; hyperuricemia and/or gout; a pro-coagulant state; atherosclerosis; or truncal obesity wherein said use can occur alone or in combination with other agents to treat the insulin resistance syndrome or individual aspects of the insulin resistance syndrome.
IT 169939-94-0, LY333531
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of insulin resistance syndrome)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L54 ANSWER 12 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 12 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:83048 CAPLUS
DOCUMENT NUMBER: 136:363557
TITLE: Inhibition of protein kinase C.beta. prevents impaired endothelium-dependent vasodilation caused by hyperglycemia in humans
AUTHOR(S): Beckman, Joshua A.; Goldfine, Allison B.; Gordon, Mary Beth; Garrett, Leslie A.; Creager, Mark A.
CORPORATE SOURCE: Cardiovascular Division, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA
SOURCE: Circulation Research (2002), 90(1), 107-111
CODEN: CIRUAL; ISSN: 0009-7330
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The bioavailability of nitric oxide is decreased in animal models and humans with diabetes mellitus. Hyperglycemia, in particular, attenuates endothelium-dependent vasodilation in healthy subjects. In vitro and in vivo animal studies implicate activation of protein kinase C.beta. as an important mechanism whereby hyperglycemia decreases endothelium-derived nitric oxide. Accordingly, this study tested the hypothesis that inhibition of protein kinase C.beta. would prevent impairment of endothelium-dependent vasodilation in healthy humans exposed to hyperglycemia. This study was a randomized, double-blind, placebo-controlled, crossover trial. Healthy subjects were treated with an orally active, selective, protein kinase C.beta. inhibitor, LY333531, or matching placebo once a day for 7 days before vascular function testing. Forearm blood flow was measured using venous-occlusion, strain-gauge plethysmog. Endothelium-dependent vasodilation was measured via incremental brachial artery administration of methacholine chloride (0.3 to 10 .mu.g/min) during euglycemia and after 6 h of hyperglycemic clamp. The forearm blood flow dose-response curve to methacholine was significantly attenuated by hyperglycemia after placebo treatment (P=0.009 by ANOVA, euglycemia vs. hyperglycemia) but not after treatment with LY333531. Inhibition of protein kinase C.beta. prevents the redn. in endothelium-dependent vasodilation induced by acute hyperglycemia in healthy humans in vivo. These findings suggest that hyperglycemia impairs endothelial function, in part, via protein kinase C.beta. activation.
IT 169939-94-0, LY333531
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of protein kinase C.beta. prevents impaired endothelium-dependent vasodilation caused by hyperglycemia in humans)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

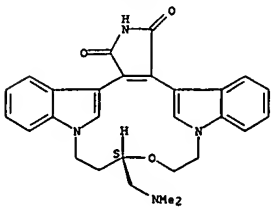
Absolute stereochemistry.

L54 ANSWER 13 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:71868 CAPLUS
DOCUMENT NUMBER: 136:112655
TITLE: Modulation of nitric oxide synthase by modulating protein kinase C (PKC)
INVENTOR(S): King, George Liang
PATENT ASSIGNEE(S): Joslin Diabetes Center, USA
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002005810	A1	20020124	WO 2001-US22514	20010718
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002048581	A1	20020425	US 2001-907012	20010717

PRIORITY APPLN. INFO.: US 2000-219246P P 20000718
AB The invention provides methods of modulating endothelial nitric oxide synthase (eNOS) expression, e.g., insulin-stimulated eNOS expression, by modulating PKC.beta.. The methods are useful in the treatment of insulin-related disorders, e.g. hypertension.
IT 169939-94-0, LY 333531
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nitric oxide synthase modulation by modulating protein kinase C)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L54 ANSWER 13 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 14 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:46023 CAPLUS
DOCUMENT NUMBER: 137:18260
TITLE: Protein kinase C and the development of diabetic vascular complications
AUTHOR(S): Way, K. J.; Katai, N.; King, G. L.
CORPORATE SOURCE: Research Division, Joslin Diabetes Center, Harvard Medical School, Boston, MA, 02215, USA
SOURCE: Diabetic Medicine (2001), 18(12), 945-959
CODEN: DIMEEV; ISSN: 0742-3071
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

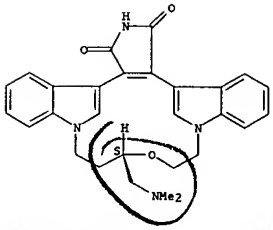
AB A review. Hyperglycemic control in diabetes is key to preventing the development and progression of vascular complications such as retinopathy, nephropathy and neuropathy. Increased activation of the diacylglycerol (DAG)-protein kinase C (PKC) signal transduction pathway has been identified in vascular tissues from diabetic animals, and in vascular cells exposed to elevated glucose. Vascular abnormalities assocd. with glucose-induced PKC activation leading to increased synthesis of DAG include altered vascular blood flow, extracellular matrix deposition, basement membrane thickening, increased permeability and neovascularization. Preferential activation of the PKC.beta. isoform by elevated glucose is reported to occur in a variety of vascular tissues. This has lead to the development of LY333531, a PKC.beta. isoform specific inhibitor, which has shown potential in animal models to be an orally effective and nontoxic therapy able to produce significant improvements in diabetic retinopathy, nephropathy, neuropathy and cardiac dysfunction. Addnl., the antioxidant vitamin E has been identified as an inhibitor of the DAG-PKC pathway, and shows promise in reducing vascular complications in animal models of diabetes. Given the overwhelming evidence indicating a role for PKC activation in contributing to the development of diabetic vascular complications, pharmacol. therapies that can modulate this pathway, particularly with PKC isoform selectivity, show great promise for treatment of vascular complications, even in the presence of hyperglycemia.

IT **169939-94-0**, LY333531
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diacylglycerol-protein kinase C signal transduction pathway in diabetic vascular complications in relation to)

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

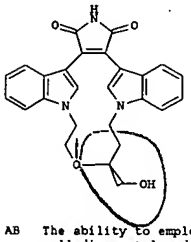
L54 ANSWER 14 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 167 THERE ARE 167 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 15 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:695739 CAPLUS
DOCUMENT NUMBER: 136:37820
TITLE: An enantioselective strategy to macrocyclic bisindolylmaleimides. An efficient formal synthesis of LY 333531
AUTHOR(S): Trost, Barry M.; Tang, Weiping
CORPORATE SOURCE: Department of Chemistry, Stanford University, Stanford, CA, 94305-5080, USA
SOURCE: Organic Letters (2001), 3(21), 3409-3411
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

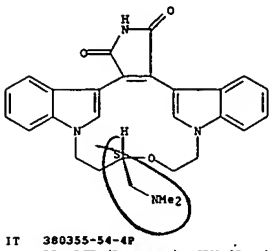
AB The ability to employ a bromo alc. as a nucleophile in a palladium-catalyzed dynamic kinetic asym. transformation leads to an efficient synthesis of a selective PKC inhibitor under clin. development. Thus, palladium-catalyzed alkylation of butadiene monoepoxide with BrCH2CH2OH gave a chiral alc., which was converted in 7 steps to the desired macrocyclic LY 333531 precursor (I).

IT **169939-94-0P**, LY 333531
RL: PNU (Preparation, unclassified); PREP (Preparation)
(asym. synthesis of LY 333531)

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

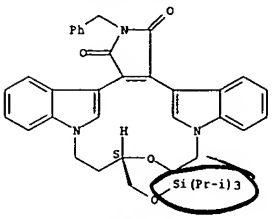
Absolute stereochemistry.

L54 ANSWER 15 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



IT 380355-54-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(asym. synthesis of LY 333531)
RN 380355-54-4 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-19-(phenylmethyl)-9-[[[tris(1-methylethyl)silyl]oxy]methyl]-, (9S)- (9CI) (CA INDEX NAME)

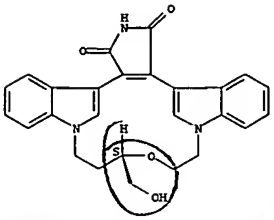
Absolute stereochemistry.



IT 169940-55-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(asym. synthesis of LY 333531)
RN 169940-55-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(hydroxymethyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 15 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 16 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:180067 CAPLUS
DOCUMENT NUMBER: 134:340494
TITLE: Cyclization strategies for the synthesis of macrocyclic bisindolylmaleimides
AUTHOR(S): Faul, Margaret M.; Krumrich, Christine A.
CORPORATE SOURCE: Chemical Process Research and Development Division, Lilly Research Laboratories A Division of Eli Lilly and Company, Indianapolis, IN, 46285-4813, USA
SOURCE: Journal of Organic Chemistry (2001), 66(6), 2024-2033
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:340494
GI

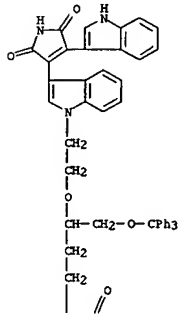
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Three new approaches to the synthesis of macrocyclic bisindolylmaleimides I (R = Me2N, pyrrolidino, PhCH2NH, MeNH) have been identified. Two strategies afford macrocycle II (R = Ph3C, PhCH2), the penultimate intermediate for the synthesis of I, in 73% and 32% yield by intramol. cyclization of III [R1 = Ph3COCH2CH(BrCH2CH2)O, Ph3COCH2CH(PhCH2OCH2)O], resp. The optimum synthesis of I (R = Me2N) was achieved in nine steps and 15% yield by intramol. formation of the macrocycle and maleimide in one step by reaction of the sodium salt of indole-3-acetamide with Me indole-3-glyoxylate IV. The mechanism of this reaction has been elucidated, using the trityl-protected deriv., to involve initial formation of an intermediate tricarbonyl imide, followed by irreversible alkylation of the indole nitrogen to generate the 17-membered macrocycle. Cyclization of the macrocycle to an intermediate hydroxymaleimide and subsequent dehydration afforded II (R = Ph3C). This approach eliminated the problem of dimerization obsd. in the intramol. cyclization reactions.

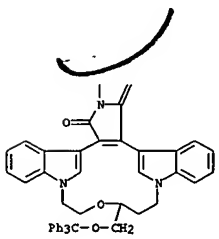
IT 336883-66-0P 336883-77-3P
RL: BYP (Byproduct); PREP (Preparation)
(byproduct in the prepn. of bisindolylmaleimide macrocycles by condensation of substituted indoleglyoxalates and indoleacetamides followed by macrocyclization)
RN 336883-66-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 19-[3-[2-[3-[2,5-dihydro-4-(1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]-1H-indol-1-yl]ethoxy]-4-(triphenylmethoxy)butyl]-6,7,10,11-tetrahydro-9-[(triphenylmethoxy)methyl]- (9CI) (CA INDEX NAME)

L54 ANSWER 16 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-A



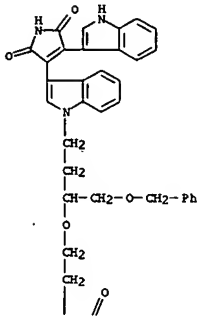
PAGE 2-A



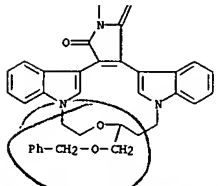
RN 336883-77-3 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 19-[2-[3-[3-[2,5-dihydro-4-(1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]-1H-indol-1-yl]-1-[4-(phenylmethoxy)methyl]propoxy]ethyl]-6,7,10,11-tetrahydro-9-[(phenylmethoxy)methyl]- (9CI) (CA INDEX NAME)

L54 ANSWER 16 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-A

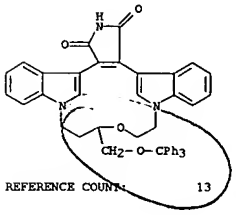


PAGE 2-A



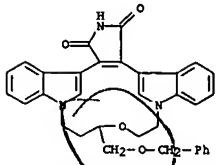
IT 336883-76-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of bisindolylmaleimide macrocycles by condensation of substituted indoleglyoxalates and indoleacetamides followed by macrocyclization)
RN 336883-76-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[(phenylmethoxy)methyl]- (9CI) (CA INDEX NAME)

L54 ANSWER 16 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

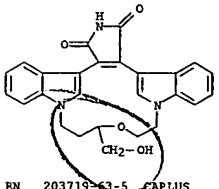


REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 16 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



IT 169939-87-1P 203719-63-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of bisindolylmaleimide macrocycles by condensation of substituted indoleglyoxalates and indoleacetamides followed by macrocyclization)
RN 169939-87-1 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(hydroxymethyl)- (9CI) (CA INDEX NAME)



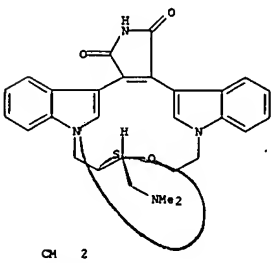
RN 203719-63-5 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[(triphenylmethoxy)methyl]- (9CI) (CA INDEX NAME)

L54 ANSWER 17 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:8786 CAPLUS
DOCUMENT NUMBER: 135:55276
TITLE: LY-333531 mesylate hydrate: symptomatic antidiabetic; protein kinase C inhibitor
AUTHOR(S): Sorbera, L. A.; Silvestre, J.; Rabasseda, X.; Castaner, J.
CORPORATE SOURCE: Prous Science, Barcelona, 08080, Spain
SOURCE: Drugs of the Future (2000), 25(10), 1017-1026
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 63 refs. regarding the drug LY-333531 mesylate hydrate, a symptomatic antidiabetic drug and protein kinase C inhibitor. Topics discussed include its synthesis; pharmacol. actions; pharmacokinetics; and clin. studies.
IT 202260-21-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LY-333531 mesylate hydrate a symptomatic antidiabetic and protein kinase C inhibitor)
RN 202260-21-7 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)-, monomethanesulfonate, monohydrate (9CI) (CA INDEX NAME)

CM 1

CRN 169939-94-0
CMF C28 H28 N4 O3

Absolute stereochemistry.



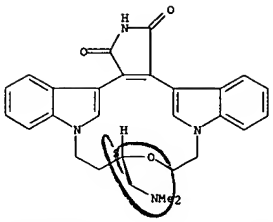
CM 2

CRN 75-75-2
CMF C H4 O3 S

L54 ANSWER 17 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 18 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 18 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:903769 CAPLUS
DOCUMENT NUMBER: 135:14147
TITLE: Impact of PKC .beta. inhibitor on diabetic complications
AUTHOR(S): Nawata, Hajime; Inoguchi, Toyoshi; Ishii, Hidehiro; Kunisaki, Makoto; Yanauchi, Teruaki; Umeda, Fumio
CORPORATE SOURCE: Department of Medicine and Bioregulatory Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, 812-8582, Japan
SOURCE: International Congress Series (2000), 1209, 61-65
CODEN: EXMDA4; ISSN: 0531-5131
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Recent studies have indicated that hyperglycemia and diabetes exert its adverse effects on vascular tissues by activating the diacylglycerol (DAG)- protein kinase C (PKC) pathway. Among various PKC isoforms, PKC .beta. isoform was preferentially activated in the retina, kidney, aorta, and heart of diabetic animal models. Activation of PKC .beta. isoform may cause functional and pathol. changes found in diabetic vascular tissues. To test this hypothesis, the authors exam. the effects of PKC .beta. isoform-specific inhibitor on various vascular dysfunctions in diabetic rats. Abnormal retinal and renal hemodynamics and the increase in albuminuria in diabetic rats were ameliorated by PKC .beta. inhibitor treatment. Conduction disturbance due to impaired gap junction activity in heart from diabetic rats was also normalized by this inhibitor treatment. These evidences strongly suggest that PKC .beta. inhibitor may normalize some of vascular dysfunctions assocd. with diabetes and thus prevent the development of diabetic vascular complications.
IT 169939-94-0, Ly333531
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(impact of PKC .beta. inhibitor on diabetic complications)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 19 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:645802 CAPLUS
DOCUMENT NUMBER: 133:217700
TITLE: Inhibition of protein kinase C to treat permeability failure in peritoneal dialysis for kidney failure
INVENTOR(S): King, George Liang
PATENT ASSIGNEE(S): Joslin Diabetes Center, Inc., USA
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

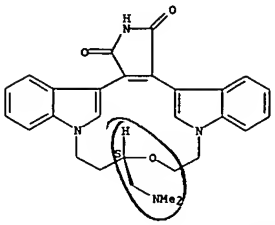
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000053013	A1	20000914	WO 2000-US6405	20000310

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-124043P P 19990312
AB The invention features a method of treating a subject having a permeability disjunction whereby an inhibitor of PKC (protein kinase C), e.g. PKC .beta., is added to the peritoneal dialysis fluid and administered to a subject having renal failure. The invention also features an improved peritoneal dialysis fluid and methods of making such dialysis fluid.
IT 169939-94-0, LY333531
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein kinase C inhibition to treat permeability failure in peritoneal dialysis for kidney failure)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 19 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 20 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN

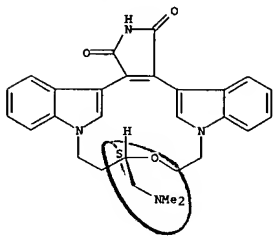
ACCESSION NUMBER: 2000:575229 CAPLUS
DOCUMENT NUMBER: 133:361638
TITLE: Macrovascular complications as risk factors for diabetic retinopathy. Diabetic retinopathy and cytokines
AUTHOR(S): Umeda, Fumio; Kunisaki, Makoto
CORPORATE SOURCE: Department of Medicine and Bioregulatory Science, Graduate School of Medical Science, Kyushu University, Japan
SOURCE: Ganki (2000), 51(3), 274-278
CODEN: GNKIEX; ISSN: 0015-5667
PUBLISHER: Nippon Ganka Kiyokai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB Hyperglycemia-induced diacylglycerol (DAG)-protein kinase C (PKC) activation is a causal factor in the development of diabetic retinopathy. The activation of PKC changes prodn. of various growth factors and cytokines such as vascular endothelial growth factor (VEGF), transforming growth factor (TGF .beta.), interleukin 1-.beta. (IL 1-.beta.), leading abnormalities of retinal permeability, blood flow, cell proliferation, and neovascularization. Administration of d-.alpha.-tocopherol, which decreases DAG level, possibly through the activation of DAG kinase, prevents development of diabetic retinopathy. In addn., the inhibition of PKC .beta., isoform by a specific inhibitor (LY333531) can normalize PKC activation and cytokines abnormalities.

IT **169939-94-0**, LY333531
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(macrovascular complications as risk factors for diabetic retinopathy)

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L54 ANSWER 20 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

L54 ANSWER 21 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN

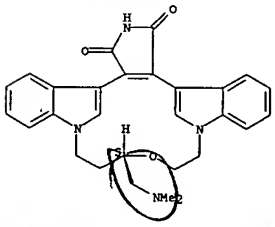
ACCESSION NUMBER: 2000:566720 CAPLUS
DOCUMENT NUMBER: 134:248
TITLE: Enzymatic rationale and preclinical support for a potent protein kinase C.beta. inhibitor in cancer therapy
AUTHOR(S): Teicher, Beverly A.; Alvarez, Enrique; Mendelsohn, Laurane G.; Ara, Gulshan; Menon, Krishna; Ways, D. Kirk
CORPORATE SOURCE: Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, IN, 46285, USA
SOURCE: Advances in Enzyme Regulation (1999), 39, 313-327
CODEN: AEZRA2; ISSN: 0065-2571
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The antitumor activity of LY333531 alone and in combination with cytotoxic antitumor agents in in-vivo models of non-small cell lung cancer and brain cancer were studied.

IT **169939-94-0**, LY333531
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(enzymic rationale and preclin. support for a potent PKC.beta. inhibitor in cancer therapy)

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

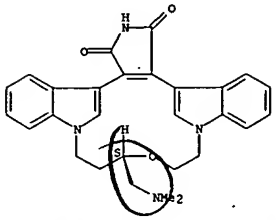


REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 22 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:522258 CAPLUS
DOCUMENT NUMBER: 133:246805
TITLE: Three- and four-dimensional-quantitative structure activity relationship (3D/4D-QSAR) analyses of CYP2C9 inhibitors
AUTHOR(S): Ekins, Sean; Bravi, Gianpaolo; Binkley, Shelly; Gillespie, Jennifer S.; Ring, Barbara J.; Wikel, James H.; Wrighton, Steven A.
CORPORATE SOURCE: Department of Drug Disposition, Lilly Research Laboratories, Lilly Corporate Center, Eli Lilly and Co., Indianapolis, IN, 46285, USA
SOURCE: Drug Metabolism and Disposition (2000), 28(8), 994-1002
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The interaction of competitive type inhibitors with the active site of cytochrome P 450 (CYP) 2C9 has been predicted using three- and four-dimensional quant. structure activity relationship (3D-/4D-QSAR) models constructed using previously unreported and literature-derived data. 3D-QSAR pharmacophore models of the common structural features of CYP2C9 inhibitors were built using the program Catalyst and compared with 3D- and 4D-QSAR partial least-squares models, which use mol. surface-weighted holistic invariant mol. descriptors of the size and shape of inhibitors. The Catalyst models generated from multiple conformers of competitive inhibitors of CYP2C9 activities contained at least one hydrophobic and two hydrogen bond acceptor/donor regions. Catalyst model 1 was constructed with Ki(apparent) values for inhibitors of tolbutamide and diclofenac 4'-hydroxylation (n = 9). Catalyst model 2 was generated from literature Ki(apparent) values for (S)-warfarin 7-hydroxylation (n = 29), and Catalyst model 3 from literature IC50 values for tolbutamide 4-hydroxylation (n = 13). These three models illustrated correlation values of obsd. and predicted inhibition for CYP2C9 of r = 0.91, 0.89, and 0.71, resp. Catalyst pharmacophores generated with Ki(apparent) values were validated by predicting the Ki(apparent) value of a test set of CYP2C9 inhibitors also derived from the literature (n = 14). Twelve of fourteen of these Ki(apparent) values were predicted to be within 1 log residual of the obsd. value using Catalyst model 1, whereas Catalyst model 2 predicted 10 of 14 Ki(apparent) values. The corresponding partial least-squares mol. surface-weighted holistic invariant mol. 3D- and 4D-QSAR models for all CYP2C9 data sets yielded predictable models as assessed using cross-validation. These 3D- and 4D-QSAR models of CYP inhibition will aid in future prediction of drug-drug interactions.
IT 169939-94-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(three- and four-dimensional-quant. structure activity relationship analyses of CYP2C9 inhibitors)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

L54 ANSWER 22 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

Absolute stereochemistry.

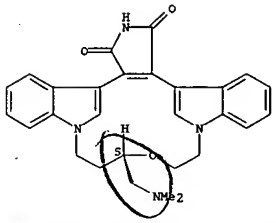


REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 23 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:258256 CAPLUS
DOCUMENT NUMBER: 133:37993
TITLE: Amelioration of accelerated diabetic mesangial expansion by treatment with a PKC .beta. inhibitor in diabetic db/db mice, a rodent model for type 2 diabetes
AUTHOR(S): Koya, Daisuke; Haneda, Masakazu; Nakagawa, Hiroko; Isshiki, Keiji; Sato, Haruhisa; Maeda, Shiro; Sugimoto, Toshiro; Yasuda, Hitoshi; Kashiwagi, Atsunori; Ways, D. Kirk; King, George L.; Kikkawa, Ryuichi
CORPORATE SOURCE: Third Department of Medicine, Shiga University of Medical Science, Shiga, 520-2192, Japan
SOURCE: FASEB Journal (2000), 14(3), 439-447
CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Activation of protein kinase C (PKC) is implicated as an important mechanism by which diabetes causes vascular complications. We have recently shown that a PKC .beta. inhibitor ameliorates not only early diabetes-induced glomerular dysfunction such as glomerular hyperfiltration and albuminuria, but also overexpression of glomerular mRNA for transforming growth factor .beta.1 (TGF-.beta.1) and extracellular matrix (ECM) proteins in streptozotocin-induced diabetic rats, a model for type 1 diabetes. In this study, we examd. the long-term effects of a PKC .beta. inhibitor on glomerular histol. as well as on biochem. and functional abnormalities in glomeruli of db/db mice, a model for type 2 diabetes. Administration of a PKC .beta. inhibitor reduced urinary albumin excretion rates and inhibited glomerular PKC activation in diabetic db/db mice. Administration of a PKC .beta. inhibitor also prevented the mesangial expansion obsd. in diabetic db/db mice, possibly through attenuation of glomerular expression of TGF-.beta. and ECM proteins such as fibronectin and type IV collagen. These findings provide the first in vivo evidence that the long-term inhibition of PKC activation in the renal glomeruli can ameliorate glomerular pathologies in diabetic state, and thus suggest that a PKC .beta. inhibitor might be an useful therapeutic strategy for the treatment of diabetic nephropathy.
IT 169939-94-0, LY333531
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amelioration of accelerated diabetic mesangial expansion by treatment with a PKC .beta. inhibitor, LY333531 in diabetic db/db mice, a rodent model for type 2 diabetes)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 23 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 24 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:233692 CAPLUS
DOCUMENT NUMBER: 133:140005
TITLE: Salt form selection and characterization of LY333531 mesylate monohydrate
AUTHOR(S): Engel, G. L.; Farid, N. A.; Faul, M. M.; Richardson, L. A.; Winneroski, L. L.
CORPORATE SOURCE: Biopharmaceutics Department, Lilly Research Laboratories, A Division of Eli Lilly and Company, Indianapolis, IN, USA
SOURCE: International Journal of Pharmaceutics (2000), 198(2), 239-247
CODEN: IJPHDE; ISSN: 0378-5173
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

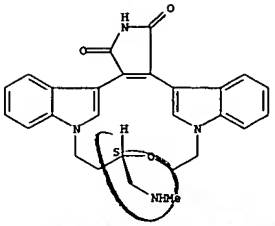
AB LY333531 is a potent protein kinase C.beta. (PKC.beta.) inhibitor currently under development for the treatment of diabetic complications. Seven salts of LY333531 (hydrochloride, sulfate, mesylate, succinate, tartrate, acetate and phosphate) were evaluated during the early phase of development. Phys. property screening techniques including microscopy, DSC, TGA, XRPD, hygroscopicity and soly. were utilized to narrow the selection to 2 salts: the mesylate and hydrochloride. Identification of the optimal salt form was based upon soly., bioavailability, phys. stability and purity. During the evaluation process three hydrated forms (anhydrate, monohydrate, and tetrahydrate) of the hydrochloride salt were identified. The mesylate salt was found to give only one, a monohydrate. Processing parameters (e.g. filtration rate, crystal form stability) demonstrated that the anhydrate was the preferred form of the hydrochloride salt. Bioavailability studies in dogs indicated that the Cmax and area under the plasma concn. vs. time curve for LY333531 and its active metabolite, LY338522, following administration of the mesylate salt were approx. 2.6-fold those obtained after the LY333531-HCl dose. This difference was presumed to be due primarily to the fact that the mesylate was 5-fold more sol. than the hydrochloride salt in water. These factors led to selection and development of LY333531 mesylate monohydrate as the active pharmaceutical ingredient for clin. evaluation.

IT **191848-32-5**, LY 338522
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(characterization and bioavailability of of LY333531 mesylate monohydrate and other salts)

RN 191848-32-5 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[(methylamino)methyl]-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

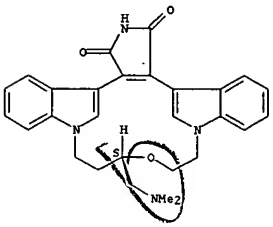
L54 ANSWER 24 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



IT **169939-93-9P 202260-21-7P 286453-43-8P 286453-44-9P**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(characterization and bioavailability of of LY333531 mesylate monohydrate and other salts)

RN 169939-93-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-{(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, (9S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

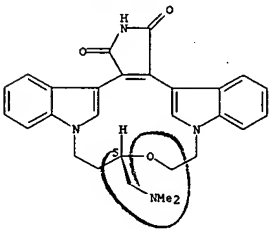
RN 202260-21-7 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-

L54 ANSWER 24 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)-, monomethanesulfonate, monohydrate (9CI) (CA INDEX NAME)

CM 1

CRN 169939-94-0
CMF C28 H28 N4 O3

Absolute stereochemistry.



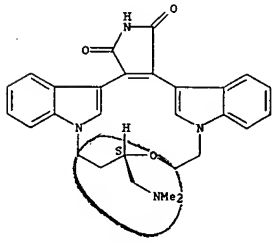
CM 2

CRN 75-75-2
CMF C H4 O3 S

RN 286453-43-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, monohydrate, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 24 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

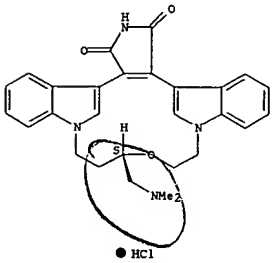


● H_2O

● HCl

RN 286453-44-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, tetrahydrate, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●4 H_2O

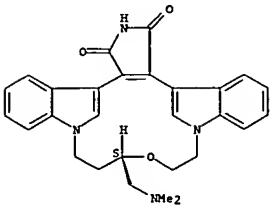
● HCl

IT **169939-94-0**, LY333531
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(characterization and bioavailability of of LY333531 mesylate monohydrate and other salts)

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-

L54 ANSWER 24 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

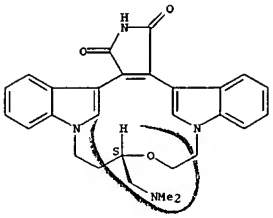
L54 ANSWER 25 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:690783 CAPLUS
DOCUMENT NUMBER: 131:303390
TITLE: Therapeutic treatment for renal dysfunction comprising protein kinase C inhibitor
INVENTOR(S): Ways, Douglas Kirk; Gilbert, Richard
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 951903	A1	19991027	EP 1999-200660	19990305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6225301	B1	20010501	US 1999-253718	19990222
ZA 9901784	A	19991213	ZA 1999-1784	19990305

PRIORITY APPLN. INFO.: US 1998-76852P P 19980305
OTHER SOURCE(S): MARPAT 131:303390
AB A method for treating renal dysfunctions is disclosed, particularly using the isoenzyme selective PKC inhibitor, (S)-3,4-[N,N'-1,1'-((2'-ethoxy)-3'-(O)-4'-(N,N-dimethylamino)-butane)-bis-(3,3'-indolyl)]-1(H)-pyrrole-2,5-dione hydrochloride salt (I). A hard gelatin capsule contained I 5, starch 200, and magnesium stearate 10 mg.
IT 169939-93-9 169939-94-0
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(therapeutic treatment for renal dysfunction comprising protein kinase C inhibitor)
RN 169939-93-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

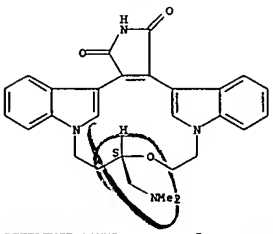
L54 ANSWER 25 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



● HCl

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

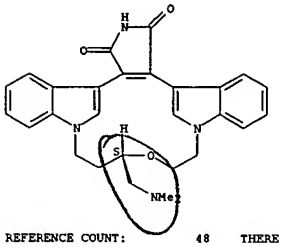


REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 26 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:644025 CAPLUS
DOCUMENT NUMBER: 131:331953
TITLE: A protein kinase C-.beta.-selective inhibitor ameliorates neural dysfunction in streptozotocin-induced diabetic rats
AUTHOR(S): Nakamura, Jiro; Kato, Koichi; Hamada, Yoji; Nakayama, Mikihiro; Chaya, Sadao; Nakashima, Eitaro; Naruse, Keiko; Kasuya, Yasuhide; Mizubayashi, Ryuichi; Miwa, Kazuma; Yasuda, Yutaka; Kamiya, Hideki; Ienaga, Kazuharu; Sakakibara, Fumihiko; Koh, Naoki; Hotta, Nigishi
CORPORATE SOURCE: Third Department of Internal Medicine, Nagoya University School of Medicine, Nagoya, 466-8550, Japan
SOURCE: Diabetes (1999), 48(10), 2090-2095
CODEN: DIAEAZ; ISSN: 0012-1797
PUBLISHER: American Diabetes Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Increased protein kinase C (PKC) activity has been implicated in the pathogenesis of diabetic retinopathy and nephropathy. However, the role of PKC in diabetic neuropathy remains unclear. The present study was conducted to compare the effect of PKC inhibition by a PKC-.beta.-selective inhibitor, LY333531 (LY), on diabetic nerve dysfunction with that of an aldose reductase inhibitor, NZ-314 (NZ). Streptozotocin-induced diabetic rats were treated with or without LY and/or NZ for 4 wk, and motor nerve conduction velocity (MNCV), coeff. of variation of R-R interval (CVR-R), sciatic nerve blood flow (SNBF), peak latencies of oscillatory potentials on electroretinogram, PKC activities in membranous and cytosolic fractions of sciatic nerves, and polyol contents in the tail nerves were measured. Untreated diabetic rats demonstrated delayed MNCV, decreased CVR-R, reduced SNBF, and prolonged peak latencies of oscillatory potentials. Treatment with LY as well as NZ prevented all these deficits in diabetic rats. There were no significant differences in PKC activities in membranous or cytosolic fractions of sciatic nerves between normal and diabetic rats. Treatment with neither LY nor NZ altered PKC activities. Nerve myo-inositol depletion in diabetic rats was ameliorated not only by NZ, but also by LY. These observations suggest that inhibition of PKC-.beta. by LY may have a beneficial effect in preventing the development of diabetic nerve dysfunction, and that this effect may be mediated through its action on the endoneurial micro-vasculature.
IT 169939-94-0, LY333531
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein kinase C-.beta.-selective inhibitor ameliorates neural dysfunction in streptozotocin-induced diabetic rats)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 26 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

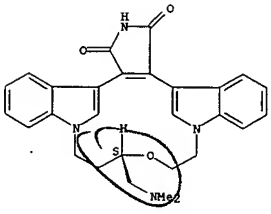


REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 27 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:635012 CAPLUS
DOCUMENT NUMBER: 132:146140
TITLE: Three and four dimensional-quantitative structure activity relationship (3D/4D-QSAR) analyses of CYP2D6 inhibitors
AUTHOR(S): Ekins, Sean; Bravi, Gianpaolo; Binkley, Shelly; Gillespie, Jennifer S.; Ring, Barbara J.; Wikel, James H.; Wrighton, Steven A.
CORPORATE SOURCE: Departments of Drug Disposition, Lilly Research Laboratories, Eli Lilly and Co., Lilly Corporate Center, Indianapolis, IN, 46285, USA
SOURCE: Pharmacogenetics (1999), 9(4), 477-489
CODEN: PHMCEE; ISSN: 0960-314X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Three- and four-dimensional quant. structure activity relationship (3D/4D-QSAR) pharmacophore models of competitive inhibitors of CYP2D6 were constructed using data from our lab. or the literature. The 3D-QSAR pharmacophore models of the common structural features of CYP2D6 inhibitors were built using the program Catalyst (Mol. Simulations, San Diego, CA, USA). These 3D-QSAR models were compared with 3D and 4D-QSAR partial least squares (PLS) models which were constructed using mol. surface-weighted holistic invariant mol. (MS-WHIM) descriptors of size and shape of inhibitors. The first Catalyst model was generated from multiple conformers of competitive inhibitors (n = 20) of CYP2D6 mediated bufurolol 1'-hydroxylation. This model demonstrated a correlation of obsd. and predicted Ki (apparent) values of r = 0.75. A second Catalyst model was constructed from literature derived Ki (apparent) values (n = 31) for the inhibition of CYP2D6. This model provided a correlation of obsd. and predicted inhibition for CYP2D6 of r = 0.91. Both Catalyst Ki pharmacophores were then validated by predicting the Ki (apparent) of a test set of known CYP2D6 inhibitors (n = 15). Ten out of 15 of these Ki (apparent) values were predicted to be within one log residual of the obsd. value using our CYP2D6 inhibitor model, while the literature model predicted nine out of 15 values. Similarly, 3D- and 4D-QSARs derived from PLS MS-WHIM for our dataset yielded predictable models as assessed using cross-validation. The corresponding cross-validated PLS MS-WHIM model for the literature dataset yielded a comparable 3D-QSAR and improved 4D-QSAR value. Such computational models will aid in future prediction of drug-drug interactions.
IT **169939-94-0**, Ly333531
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3D/4D-QSAR analyses of CYP2D6 inhibitors)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 27 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 28 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:579498 CAPLUS
DOCUMENT NUMBER: 131:194293
TITLE: Use of protein kinase C (PKC) inhibitors for the manufacture of a medicament for the treatment of asthma
INVENTOR(S): Ways, Douglas Kirk
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 940143	A2	19990908	EP 1999-200662	19990305
EP 940143	A3	19990922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6103712	A	20000815	US 1999-253716	19990222
ZA 9901786	A	19990906	ZA 1999-1786	19990305

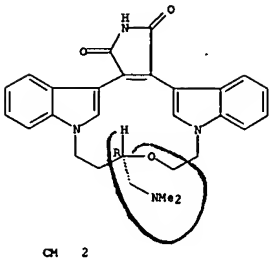
PRIORITY APPLN. INFO.: US 1998-76850P P 19980305
OTHER SOURCE(S): MARPAT 131:194293
AB A method for treating asthma and disease conditions assocd. therewith is disclosed, particularly using the isoenzyme selective PKC inhibitor, (S)-3,4-{N, N'-1,1'-{(2"-ethoxy)-3"'(O)-4"'-(N,N-dimethylamino)-butane}-bis-(3,3'-indolyl)}-1(H)-pyrrole-2,5-dione and its pharmaceutically acceptable salts.
IT **242128-71-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase C inhibitors for asthma treatment)
RN 242128-71-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9R)-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 169940-29-8
CMF C28 H28 N4 O3

Absolute stereochemistry.

L54 ANSWER 28 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



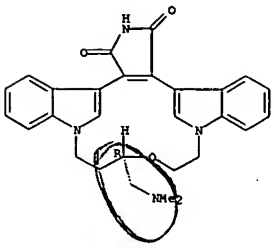
CM 2

CRN 75-75-2
CMF C H4 O3 S

IT 169940-29-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein kinase C inhibitors for asthma treatment)
RN 169940-29-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 28 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



L54 ANSWER 29 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:579497 CAPLUS
DOCUMENT NUMBER: 131:194277
TITLE: Use of protein kinase C (PKC) inhibitors for the manufacture of a medicament for the treatment of cytomegalovirus infection
INVENTOR(S): Ways, Douglas Kirk
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 940141	A2	19990908	EP 1999-200659	19990305
EP 940141	A3	19990929		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6291446	B1	20010918	US 1999-253700	19990222
ZA 9901785	A	19990906	ZA 1999-1785	19990305

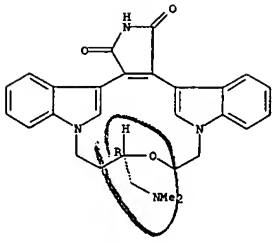
PRIORITY APPLN. INFO.: US 1998-76857P P 19980305
OTHER SOURCE(S): MARPAT 131:194277
AB A method for treating CMV infection and disease conditions assocd. therewith is disclosed, particularly using the isoenzyme selective PKC inhibitor, (S)-3,4-[N,N'-1,1'-((2"-ethoxy)-3"'(O)-4"'-(N,N-dimethylamino)-butane)- bis-(3,3'-indolyl)]-1(H)-pyrrole-2,5-dione hydrochloride salt.
IT 242128-71-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase C inhibitors for treatment of cytomegalovirus infection)
RN 242128-71-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9R)-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 169940-29-8
CMF C28 H28 N4 O3

Absolute stereochemistry.

L54 ANSWER 29 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



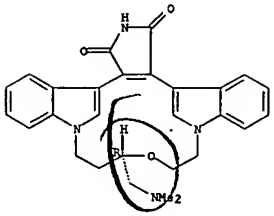
CM 2

CRN 75-75-2
CMF C H4 O3 S

IT 169940-29-8 190265-61-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein kinase C inhibitors for treatment of cytomegalovirus infection)
RN 169940-29-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9R)- (9CI) (CA INDEX NAME)

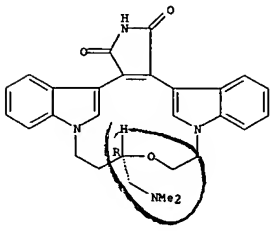
Absolute stereochemistry.

L54 ANSWER 29 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 190265-61-3 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, (9R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L54 ANSWER 30 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:576780 CAPLUS
DN 131:194285
TI Use of protein kinase C (PKC) inhibitors for the manufacture of a medicament for the treatment of autoimmune diseases
IN Ways, Douglas Kirk; Wierda, Daniel
PA Eli Lilly and Co., USA
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
PI

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9944607	A1	19990910	WO 1999-US5004	19990305
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6103713	A	20000815	US 1999-253717	19990222
ZA 9901783	A	19990906	ZA 1999-1783	19990305
EP 940142	A2	19990908	EP 1999-200661	19990305
EP 940142	A3	19991006		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2323176	AA	19990910	CA 1999-2323176	19990305
AU 9930719	A1	19990920	AU 1999-30719	19990305
JP 2002505285	T2	20020219	JP 2000-534209	19990305

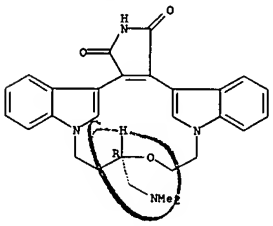
PRIORITY APPLN. INFO.: US 1998-76851P P 19980305
WO 1999-US5004 W 19990305
OTHER SOURCE(S): MARPAT 131:194285
AB Methods for inhibiting activation and/or proliferation of T cells and B cells and for treating autoimmune diseases and/or disease manifestations are disclosed, particularly using the isoenzyme selective PKC inhibitor, (S)-3,4-[N,N'-1,1'-((2''-ethoxy)-3'''(O)-4'''-(N,N-dimethylamino)-butane)-bis-(3,3'-indolyl)]-1(H)-pyrrole-2,5-dione and its pharmaceutically acceptable salts.
IT 242128-71-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase C inhibitors for treatment of autoimmune diseases)
RN 242128-71-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9R)-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

L54 ANSWER 30 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

CRN 169940-29-8
CMF C28 H28 N4 O3

Absolute stereochemistry.



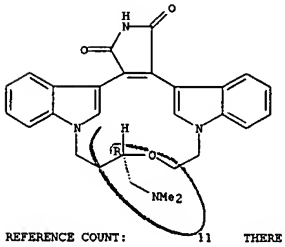
CM 2

CRN 75-75-2
CMF C H4 O3 S

IT 169940-29-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein kinase C inhibitors for treatment of autoimmune diseases)
RN 169940-29-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 30 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 31 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:576779 CAPLUS
DOCUMENT NUMBER: 131:194292
TITLE: Use of protein kinase C (PKC) inhibitors for the manufacture of a medicament for the treatment of asthma
INVENTOR(S): Ways, Douglas Kirk
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9944606	A1	19990910	WO 1999-US5003	19990305
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6103712	A	20000815	US 1999-253716	19990222
ZA 9901786	A	19990906	ZA 1999-1786	19990305
CA 2323173	AA	19990910	CA 1999-2323173	19990305
AU 9930718	A1	19990920	AU 1999-30718	19990305
JP 2002505284	T2	20020219	JP 2000-534208	19990305

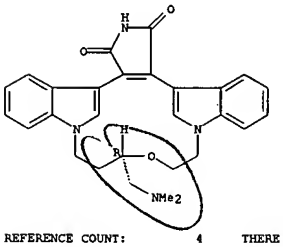
PRIORITY APPLN. INFO.: US 1998-76850P P 19980305
WO 1999-US5003 W 19990305
OTHER SOURCE(S): MARPAT 131:194292
AB A method for treating asthma and disease conditions assocd. therewith is disclosed, particularly using the isoenzyme selective PKC inhibitor, (S)-3,4-[N,N'-1,1'-((2"-ethoxy)-3"'(O)-4"'-(N,N-dimethylamino)-butane)-bis-(3,3' indolyl)]-1(H)-pyrrole-2,5-dione and its pharmaceutically acceptable salts.
IT 242128-71-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase C inhibitors for asthma treatment)
RN 242128-71-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9R)-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 169940-29-8
CMF C28 H28 N4 O3

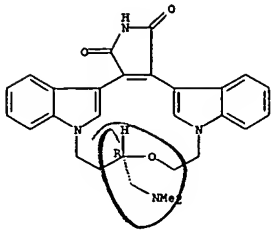
Absolute stereochemistry.

L54 ANSWER 31 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 31 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



CM 2

CRN 75-75-2
CMF C H4 O3 S

IT 169940-29-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein kinase C inhibitors for asthma treatment)
RN 169940-29-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 32 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:576778 CAPLUS
DOCUMENT NUMBER: 131:194275
TITLE: Use of protein kinase C (PKC) inhibitors for the manufacture of a medicament for the treatment of cytomegalovirus infection
INVENTOR(S): Ways, Douglas Kirk
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9944605	A1	19990910	WO 1999-US5002	19990305
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6291446	B1	20010918	US 1999-253700	19990222
ZA 9901785	A	19990906	ZA 1999-1785	19990305
CA 2323158	AA	19990910	CA 1999-2323158	19990305
AU 9930717	A1	19990920	AU 1999-30717	19990305
JP 2002505283	T2	20020219	JP 2000-534207	19990305

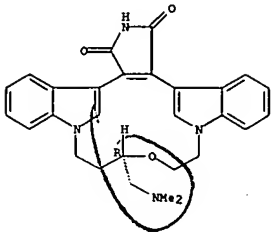
PRIORITY APPLN. INFO.: US 1998-76857P P 19980305
WO 1999-US5002 W 19990305
OTHER SOURCE(S): MARPAT 131:194275
AB A method for treating CMV infection and disease conditions assocd. therewith is disclosed, particularly using the isoenzyme selective PKC inhibitor, (S)-3,4-[N,N'-1,1'-((2"-ethoxy)-3''' (O)-4'''-(N,N-dimethylamino)-butane)-bis-(3, '-indolyl)]-1(H)-pyrrole-2,5-dione hydrochloride salt.
IT 242128-71-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase C inhibitors for treatment of cytomegalovirus infection)
RN 242128-71-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9R)-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 169940-29-8
CMF C28 H28 N4 O3

Absolute stereochemistry.

L54 ANSWER 32 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



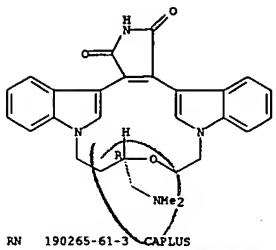
CM 2

CRN 75-75-2
CMF C H4 O3 S

IT 169940-29-8 190265-61-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein kinase C inhibitors for treatment of cytomegalovirus infection)
RN 169940-29-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9R)- (9CI) (CA INDEX NAME)

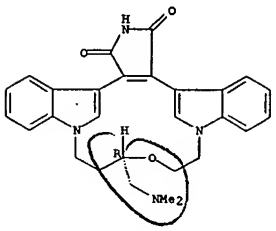
Absolute stereochemistry.

L54 ANSWER 32 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 190265-61-3 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, (9R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 33 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:576772 CAPLUS
DOCUMENT NUMBER: 131:194289
TITLE: Protein kinase C (PKC) inhibitor for treatment for renal dysfunction
INVENTOR(S): Ways, Douglas Kirk; Gilbert, Richard
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9944599	A1	19990910	WO 1999-US5447	19990305
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6225301	B1	20010501	US 1999-253718	19990222
CA 2323172	AA	19990910	CA 1999-2323172	19990305
AU 9929047	A1	19990920	AU 1999-29047	19990305
ZA 9901784	A	19991213	ZA 1999-1784	19990305
JP 2002505278	T2	20020219	JP 2000-534201	19990305

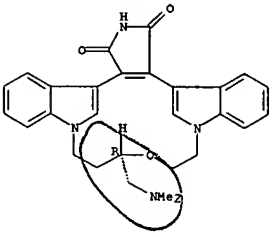
PRIORITY APPLN. INFO.: US 1998-76852P P 19980305
WO 1999-US5447 W 19990305
OTHER SOURCE(S): MARPAT 131:194289
AB A method for treating renal dysfunctions is disclosed, particularly using the isoenzyme selective PKC inhibitor, (S)-3,4-[N,N'-1,1'-[(2"-ethoxy)-3'''(O)-4'''-(N,N-dimethylamino)-butane)-bis-(3, '-indolyl)]-1(H)-pyrrole-2,5-dione hydrochloride salt.
IT 242128-71-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase C inhibitor for treatment for renal dysfunction)
RN 242128-71-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9R)-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 169940-29-8
CMF C28 H28 N4 O3

Absolute stereochemistry.

L54 ANSWER 33 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



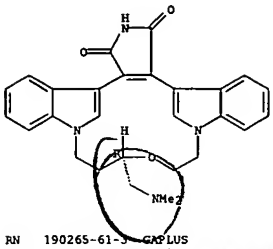
CM 2

CRN 75-75-2
CMF C H4 O3 S

IT 169940-29-8 190265-61-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein kinase C inhibitor for treatment for renal dysfunction)
RN 169940-29-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9R)- (9CI) (CA INDEX NAME)

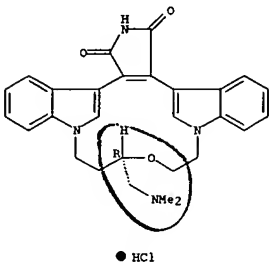
Absolute stereochemistry.

L54 ANSWER 33 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 190265-61-3 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, (9R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

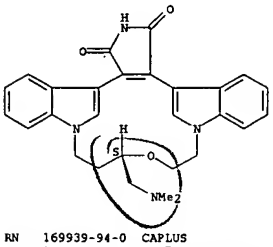


● HCl

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

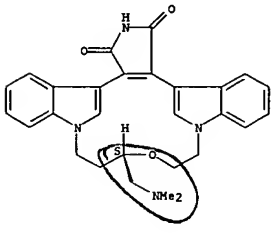
L54 ANSWER 34 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

Absolute stereochemistry.



RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L54 ANSWER 34 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:354417 CAPLUS
DOCUMENT NUMBER: 131:9633
TITLE: Protein kinase C inhibitors for treatment of chronic and acute lymphoid leukemias
INVENTOR(S): Jirousek, Michael R.; Ways, Douglas Kirk; Ballas, Lawrence M.; Straus, Lawrence E.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9926609	A2	19990603	WO 1998-US23908	19981106
WO 9926609	A3	19990826		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2311736	AA	19990603	CA 1998-2311736	19981106
AU 9913922	A1	19990615	AU 1999-13922	19981106
JP 2001523707	T2	20011127	JP 2000-521811	19981106
EP 990442	A1	20000405	EP 1998-309616	19981124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1997-66555P P 19971126
WO 1998-US23908 W 19981106
OTHER SOURCE(S): MARPAT 131:9633
AB A method for treating neoplasms assocd. with an oncogenic form of ABL gene caused by chromosome rearrangement, such as chronic lymphoid leukemia (CML) and acute lymphoid leukemia (ALL) by inducing apoptosis is disclosed, using an inhibitor of .beta.-isoenzyme of PKC. The inhibitor of the .beta.-isoenzyme of PKC is a bis-indolylmaleimide or a macrocyclic bis-indolylmaleimide, e.g. (S)-3,4-[N,N'-1,1'-((2''-ethoxy)-3'''(O)-4'''-(N,N-dimethylamino)-butane)-bis-(3,3'-indolyl)]-1(H)-pyrrole-2,5-dione and its pharmaceutically acceptable salts. A tablet was prepd. contg. an active agent 60, starch 45, microcryst. cellulose 35, PVP (as 10% soln. in water) 4, Na CM-starch 4.5, Mg stearate 0.5, and talc 1 mg/tablet, resp.
IT 169939-94-0 169939-94-0D, salts
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bisindolylmaleimides as protein kinase C inhibitors for treatment of chronic and acute lymphoid leukemias)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

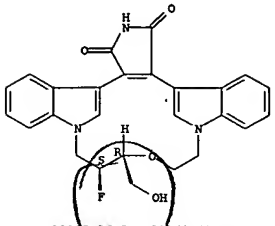
L54 ANSWER 35 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:304468 CAPLUS
DOCUMENT NUMBER: 130:352261
TITLE: Synthesis of fluorinated macrocyclic bis(indolyl)maleimides as potential 19F NMR probes for protein kinase C
AUTHOR(S): Goekjian, Peter G.; Wu, Guo-Zhang; Chen, Shi; Zhou, Lanxin; Jirousek, Michael R.; Gillig, James R.; Ballas, Lawrence M.; Dixon, Jeffrey T.
CORPORATE SOURCE: Department of Chemistry, Mississippi State University, Mississippi State, MS, 39762, USA
SOURCE: Journal of Organic Chemistry (1999), 64(12), 4238-4246
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Six macrocyclic bis(indolyl)maleimides I, II, and III (X = NMe2, OH) bearing a fluorine label on the aliph. portion of the macrocycle have been prepd. as potential fluorine NMR probes for the catalytic domain of protein kinase C. The macrocyclic bis(indolyl)maleimides such as LY333531 are reversible, ATP competitive, and isoform-selective inhibitors of protein kinase C and may thus serve to probe for subtle differences between protein kinase catalytic domains. The key stereochem. elements were put in place by a Welch aldol condensation between Et fluoroacetate and (R)-cyclohexylidene glyceraldehyde, which was followed by allylation of the secondary alc., elaboration of the alkene and ester to alcs., and mesylation. The macrocycle was formed by slow addn. of a mixt. of the fluorine-labeled aliph. dimesylate and N-Me 2,3-bis[1H-indol-3-yl]maleimide to a suspension of cesium carbonate. Adjusting the functionality led to the six fluorine-labeled macrocyclic bis(indolyl)maleimides. These compds. retain the high potency of the parent compds., with IC50 values below 5 nM for the 14-membered ring compds. I (X = NMe2, OH), II (X = NMe2) and 13-90 nM for the 15-membered ring compds. III. Vicinal proton-fluorine coupling consts. provide an exptl. parameter for detg. the local macrocycle conformation.
IT 198965-39-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and protein kinase C inhibitory activity of macrocyclic bis(indolyl)maleimides)
RN 198965-39-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 10-fluoro-6,7,10,11-tetrahydro-9-(hydroxymethyl)-, (9R,10S)- (9CI) (CA INDEX NAME)

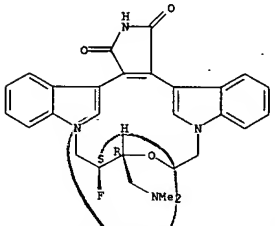
Absolute stereochemistry.

L54 ANSWER 35 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



IT **198965-36-5P 198965-60-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and protein kinase C inhibitory activity of macrocyclic bis(indolyl)maleimides)
RN 198965-36-5 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-10-fluoro-6,7,10,11-tetrahydro-, (9R,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



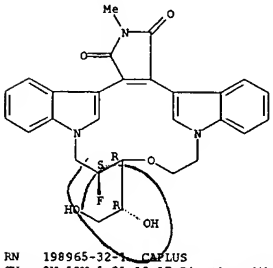
RN 198965-60-5 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-10-fluoro-6,7,10,11-tetrahydro-, (9R,10R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 35 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

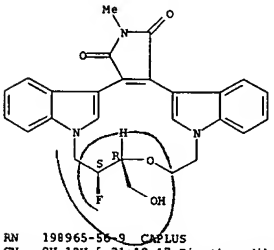
RN 198965-28-5 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(1R)-1,2-dihydroxyethyl]-10-fluoro-6,7,10,11-tetrahydro-19-methyl-, (9R,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 198965-32-1 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 10-fluoro-6,7,10,11-tetrahydro-9-(hydroxymethyl)-19-methyl-, (9R,10S)- (9CI) (CA INDEX NAME)

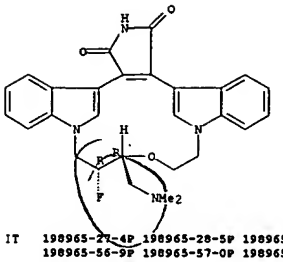
Absolute stereochemistry.



RN 198965-56-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(2R)-1,4-dioxaspiro[4.5]dec-2-yl]-10-fluoro-6,7,10,11-tetrahydro-19-methyl-, (9R,10R)- (9CI) (CA INDEX NAME)

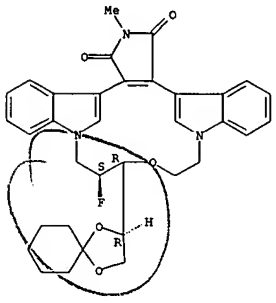
Absolute stereochemistry.

L54 ANSWER 35 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

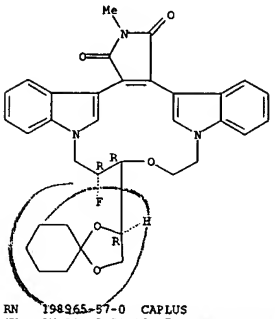


IT **198965-27-4P 198965-28-5P 198965-32-1P 198965-56-9P 198965-57-0P 198965-59-2P 198965-62-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and protein kinase C inhibitory activity of macrocyclic bis(indolyl)maleimides)
RN 198965-27-4 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(2R)-1,4-dioxaspiro[4.5]dec-2-yl]-10-fluoro-6,7,10,11-tetrahydro-19-methyl-, (9R,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

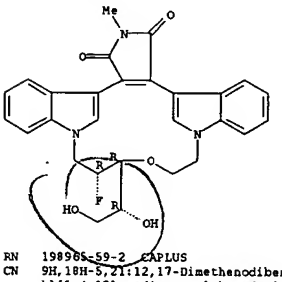


L54 ANSWER 35 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 198965-57-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(1R)-1,2-dihydroxyethyl]-10-fluoro-6,7,10,11-tetrahydro-19-methyl-, (9R,10R)- (9CI) (CA INDEX NAME)

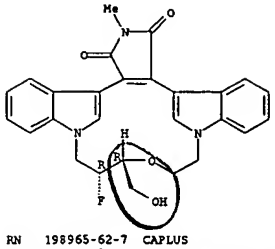
Absolute stereochemistry.



RN 198965-59-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 10-fluoro-6,7,10,11-tetrahydro-9-(hydroxymethyl)-19-methyl-, (9R,10R)- (9CI) (CA INDEX NAME)

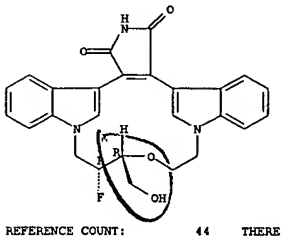
Absolute stereochemistry.

L54 ANSWER 35 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 198965-62-7 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 10-fluoro-6,7,10,11-tetrahydro-9-(hydroxymethyl)-, (9R,10R)- (9CI) (CA INDEX NAME)

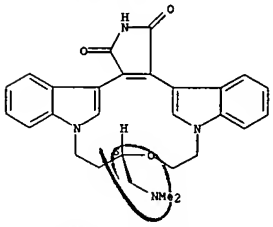
Absolute stereochemistry.



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

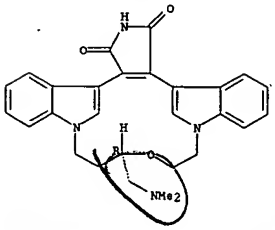
L54 ANSWER 36 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 169940-29-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



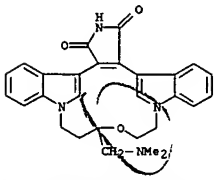
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 36 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:244205 CAPLUS
DOCUMENT NUMBER: 130:346558
TITLE: Systematic screening approach for chiral separations of basic compounds by capillary electrophoresis with modified cyclodextrins
AUTHOR(S): Liu, Li; Nussbaum, Mark A.
CORPORATE SOURCE: Pharmaceutical Sciences Division, Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, 46285, USA
SOURCE: Journal of Pharmaceutical and Biomedical Analysis (1999), 19(5), 679-694
CODEN: JPBADA; ISSN: 0731-7085
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A simple, systematic method was developed for rapidly screening potential capillary electrophoresis (CE) sepn. conditions for small, amine-contg. enantiomers. During method development, 39 pairs of enantiomers were studied and partial or complete sepn. was achieved in every case. Baseline resoln. was achieved by these initial screening conditions in over half of the cases. The screening strategy uses a bare fused silica capillary and a pH 2.5 amine-modified phosphate buffer contg. one of the selected cyclodextrins (CD): dimethyl-.beta.-CD, hydroxypropyl-.beta.-CD, hydroxypropyl-.alpha.-CD, hydroxypropyl-.gamma.-CD and sulfated-.beta.-CD. An addnl. set of compds. were screened by this approach to demonstrate the validity of the method. The paper outlines the exptl. work carried out to develop the screen and describes how one might implement it for a new compd.

IT 169939-91-7 169939-94-0 169940-29-8
RL: ANT (Analyte); PEP (Physical, engineering or chemical process); ANST (Analytical study); PROC (Process)
(systematic screening approach for chiral sepns. of amines by capillary electrophoresis using modified cyclodextrins)

RN 169939-91-7 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro- (9CI) (CA INDEX NAME)



RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-

L54 ANSWER 37 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:766507 CAPLUS
DOCUMENT NUMBER: 130:29221
TITLE: Preparation of solid porous matrixes for pharmaceutical uses
INVENTOR(S): Unger, Evan C.
PATENT ASSIGNEE(S): ImaRx Pharmaceutical Corp., USA
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9851282	A1	19981119	WO 1998-US9570	19980512
W: AU, BR, CA, CN, JP, KR, NZ				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 2002039594	A1	20020404	US 1998-75477	19980511
AU 9873787	A1	19981208	AU 1998-73787	19980512
EP 983060	A1	20000308	EP 1998-921109	19980512
R: DE, FR, GB, IT, NL				
US 2001018072	A1	20010830	US 2001-828762	20010409

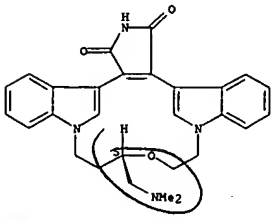
PRIORITY APPLN. INFO.: US 1997-46379P P 19970513
US 1998-75477 A 19980511
WO 1998-US9570 W 19980512

AB A solid porous matrix formed from a surfactant, a solvent, and a bioactive agent is described. Thus, amphotericin nanoparticles were prepd. by using ZrO2 beads and a surfactant. The mixt. was milled for 24 h.

IT 169939-94-0, LY333531
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of solid porous matrixes for pharmaceutical uses)

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

L54 ANSWER 37 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 38 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:719259 CAPLUS
DOCUMENT NUMBER: 129:339883
TITLE: Therapeutic treatment for skin disorders using a protein kinase C inhibitor to reduce vascular permeability
INVENTOR(S): Jirousek, Michael R.; Stramm, Lawrence E.; Vignati, Louis; Ways, Douglas K.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9848795	A1	19981105	WO 1998-US7808	19980421
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6093740	A	20000725	US 1998-57541	19980409
AU 9871318	A1	19981124	AU 1998-71318	19980421
BR 9809343	A	20000704	BR 1998-9343	19980421
JP 2002501501	T2	20020115	JP 1998-547065	19980421
EP 903145	A2	19990324	EP 1998-303403	19980430
EP 903145	A3	20010207		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 9905231	A	19991227	NO 1999-5231	19991026

PRIORITY APPLN. INFO.: US 1997-44431P P 19970430
WO 1998-US7808 W 19980421
OTHER SOURCE(S): MARPAT 129:339883

AB A method for reducing or inhibiting vascular permeability esp. the increased vascular permeability assocd. with vascular permeability factor/vascular endothelial growth factor, and dermal edema exhibited with bullous pemphigoid, erythema multiforme, dermatitis herpetiformis, contact dermatitis/delayed hypersensitivity is disclosed, particularly using the .beta.-isoenzyme selective PKC inhibitor, (S)-3,4-[N,N'-1,1'-((2"-ethoxy)-3'''(O)- 4'''-(N,N-dimethylamino)-butane)-bis-(3,3'-indolyl)]-1(H)-pyrrole-2,5-dione and its pharmaceutically acceptable salts.

IT 191937-15-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase C inhibitor to reduce vascular permeability for treatment of skin disorders)
RN 191937-15-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monomethanesulfonate (9CI)

L54 ANSWER 38 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
(CA INDEX NAME)

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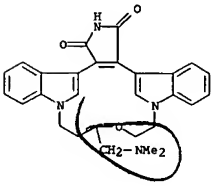
CRN 169939-91-7
CMF C28 H28 N4 O3



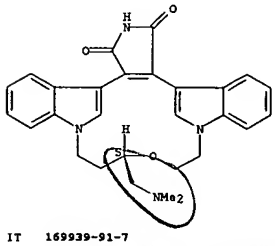
CM 2

CRN 75-75-2
CMF C H4 O3 S

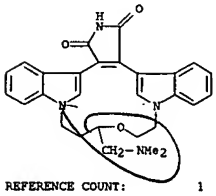
IT 169939-94-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein kinase C inhibitor to reduce vascular permeability for treatment of skin disorders)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 38 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



IT 169939-91-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; protein kinase C inhibitor to reduce vascular permeability for treatment of skin disorders)
RN 169939-91-7 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 39 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:219711 CAPLUS
DOCUMENT NUMBER: 128:290247
TITLE: Substances modulating phosphorylation of serine and threonine residues of p100/p120, and their therapeutic uses
INVENTOR(S): Staddon, James Martin; Morgan, Mary Louise; Ratcliffe, Marianne Jennifer
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan; Staddon, James Martin; Morgan, Mary Louise; Ratcliffe, Marianne Jennifer
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9814186	A1	19980409	WO 1997-GB2668	19970929
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 949917	A1	19991020	EP 1997-943070	19970929
R: DE, FR, GB				
JP 2001501618	T2	20010206	JP 1998-516314	19970929
US 6407058	B1	20020618	US 1999-280593	19990329
US 2002142943	A1	20021003	US 2002-154896	20020524

PRIORITY APPLN. INFO.: GB 1996-20390 A 19960930
WO 1997-GB2668 W 19970929
US 1999-280593 A3 19990329

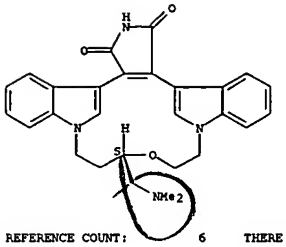
AB The degree of phosphorylation of serine and threonine residues of p100/p120 can affect the permeability of physiol. barriers and also cell-cell adhesion properties. By changing physiol. levels, various disorders can be treated, including multiple sclerosis, cancer, head injuries, edema, stroke, inflammation and gastric ulcers. Furthermore, drugs can be allowed to pass across physiol. barriers and the barriers can then be cloned.

IT 169939-94-0, LY 333531
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substances modulating phosphorylation of serine and threonine residues of p100/p120, and therapeutic use)

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 39 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

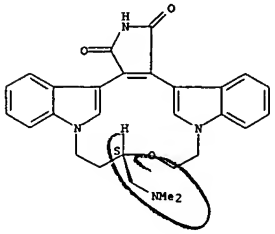
L54 ANSWER 40 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:193370 CAPLUS
DOCUMENT NUMBER: 129:39365
TITLE: Role of protein kinase C in the development of vascular disease in diabetes
AUTHOR(S): Koya, Daisuke; Kashiwagi, Atsunori
CORPORATE SOURCE: Third Dep. Med., Shiga Univ. Med. Sci., Otsu, 520-21, Japan
SOURCE: Naibunpi, Tonyobyoka (1997), 5(5), 440-447
CODEN: NATOFF; ISSN: 1341-3724
PUBLISHER: Kagaku Hyoronsha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review and discussion with 17 refs. The mechanism for activation of the diacylglycerol-protein kinase C (PKC) pathway in diabetes, activated isoforms of PKC, the importance of PKC activation in the onset of vascular complication, and effects of vitamin E and the PKC .beta. inhibitor LY333531 on diabetic vascular complications.

IT 169939-94-0, LY333531
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diabetic vascular disease response to)

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L54 ANSWER 41 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:178090 CAPLUS
DOCUMENT NUMBER: 128:221654
TITLE: Pharmaceutical compositions containing protein kinase C inhibitors for the treatment of cardiovascular diseases
INVENTOR(S): Jirousek, Michael R.; Heath, William Francis, Jr.; Ways, Douglas Kirk; Stramm, Lawrence E.
PATENT ASSIGNEE(S): Eli Lilly & Co., USA
SOURCE: U.S., 15 pp., Cont.-in-part of U.S. Ser. No. 643,706.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5723456	A	19980303	US 1996-662623	19960613
US 5624949	A	19970429	US 1995-413735	19950330
BR 9502611	A	19961001	BR 1995-2611	19950531
US 5698578	A	19971216	US 1996-734292	19961021
CA 2257693	AA	19971218	CA 1997-2257693	19970612
WO 9747298	A1	19971218	WO 1997-US9661	19970612
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9734763	A1	19980107	AU 1997-34763	19970612
AU 725582	B2	20001012		
BR 9709727	A	19990810	BR 1997-9727	19970612
EP 954308	A1	19991110	EP 1997-931034	19970612
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NZ 333341	A	20000526	NZ 1997-333341	19970612
JP 2000512293	T2	20000919	JP 1998-501674	19970612
NO 9805808	A	19990212	NO 1998-5808	19981211
KR 2000016625	A	20000325	KR 1998-710221	19981212

PRIORITY APPLN. INFO.: US 1993-163060 B2 19931207
US 1994-316973 B2 19941003
US 1995-413735 A3 19950330
US 1996-643706 A2 19960506
US 1995-457060 A1 19950601
US 1996-662623 A 19960613
WO 1997-US9661 W 19970612

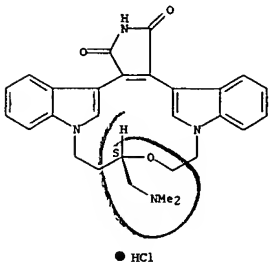
OTHER SOURCE(S): MARPAT 128:221654

AB A method for treating endothelial cell dysfunction, such as assocd. with cardiovascular disease are disclosed, particularly using the isoenzyme selective PKC inhibitor, (S)-3,4-[N,N'-1,1'-((27"-ethoxy)-3'"(0)-4'"-(N,N-dimethylamino)-butane)-bi s-(3,3'-indolyl)]-1(H)-pyrrole-2,5-dione hydrochloride salt (I). A capsule contained I 250, starch 200, and magnesium stearate 10 mg.

IT 169939-93-9 169939-94-0 169939-94-0D, acid salts
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

L54 ANSWER 41 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
(Uses)
(pharmaceutical compns. contg. protein kinase C inhibitors for treatment of cardiovascular diseases)
RN 169939-93-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, (9S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

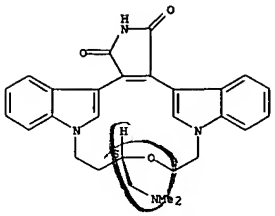


● HCl

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

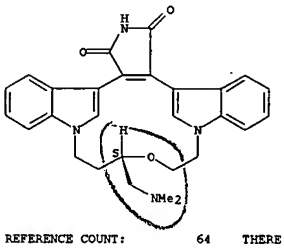
Absolute stereochemistry.

L54 ANSWER 41 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

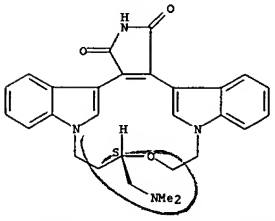


REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 42 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:162986 CAPLUS
DOCUMENT NUMBER: 128:281390
TITLE: Abnormalities of retinal metabolism in diabetes or experimental galactosemia. V. Relationship between protein kinase C and ATPases
AUTHOR(S): Kowluru, Renu A.; Jirousek, Michael R.; Stramm, Lawrence; Farid, Nagy; Engerman, Ronald L.; Kern, Timothy S.
CORPORATE SOURCE: Department of Ophthalmology and Visual Sciences, University of Wisconsin, Madison, WI, 53706-1532, USA
SOURCE: Diabetes (1998), 47(3), 464-469
CODEN: DIAEAZ; ISSN: 0012-1797
PUBLISHER: American Diabetes Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the retinas of diabetic animals, protein kinase C (PKC) activity is elevated, and Na+-K+-ATPase and calcium ATPase activities are subnormal. These abnormalities are also present in another model of diabetic retinopathy, exptl. galactosemia. The authors have investigated the relation between hyperglycemia-induced abnormalities of PKC and ATPases using a selective inhibitor of .beta. isoform of PKC (LY333531). Diabetes or exptl. galactosemia of 2 mo' duration resulted in >50% elevation of PKC activity in the retina, and administration of LY333531 prevented the elevation. In retinas of the same rats, the LY333531 prevented hyperglycemia-induced decreases of both Na+-K+-ATPase and calcium ATPase activities. Retinal microvessels, the main site of lesions in diabetic retinopathy, likewise showed elevated activity of PKC and inhibition of ATPases in diabetes and in exptl. galactosemia, and administration of LY333531 to diabetic animals prevented these abnormalities. PKC activity in sciatic nerves, in contrast, became subnormal in diabetes and exptl. galactosemia, and LY333531 had no effect on PKC activity in the sciatic nerve. PKC activity in the cerebral cortex was not affected by diabetes or exptl. galactosemia. Apparently, diabetes-induced redns. in Na+-K+-ATPase and calcium ATPase in the retina are mediated in large part by PKC-.beta.. The availability of an agent that can normalize the hyperglycemia-induced increase in PKC activity in the retina should facilitate investigation of the role of PKC in the development of diabetic retinopathy.
IT 169939-94-0, LY333531
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(redns. in Ca2+- and Na+-K+-ATPase activities in the retina in both galactosemia and hyperglycemia-induced diabetes mellitus are mediated by protein kinase C .beta. isoform)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 42 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 43 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:161133 CAPLUS
DOCUMENT NUMBER: 128:221638
TITLE: Pharmaceutical compositions containing inhibitors of PKC for the treatment of central nervous system diseases associated with HIV infection
INVENTOR(S): Jirousek, Michael R.; Ways, Douglas K.; Stramm, Lawrence E.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9808510	A1	19980305	WO 1997-US15583	19970828
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9742506	A1	19980319	AU 1997-42506	19970828
BR 9711375	A	19990817	BR 1997-11375	19970828
CN 1231607	A	19991013	CN 1997-198158	19970828
EP 834313	A1	19980408	EP 1997-306716	19970901
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 9900947	A	19990428	NO 1999-947	19990226
KR 2000035863	A	20000626	KR 1999-701558	19990226

PRIORITY APPLN. INFO.: US 1996-24869P P 19960830
US 1997-917362 A 19970826
WO 1997-US15583 W 19970828

OTHER SOURCE(S): MARPAT 128:221638

AB A compn. for treating central nervous system assocd. with HIV infection is disclosed, particularly using the isoenzyme selective PKC inhibitor, (S)-3,4-[N,N'-1,1'-((2''-ethoxy)-3'''(O)-4'''-(N,N -dimethylamino)-butane)-bis-(3,3'-indolyl)]-1(H)-pyrrole-2,5-dione hydrochloride salt (I). A gelatin capsule contained I 5, starch 200, and magnesium stearate 10 mg.

IT 169939-93-9 169939-94-0 192050-59-2
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. contg. inhibitors of PKC for treatment of central nervous system diseases assocd. with HIV infection)

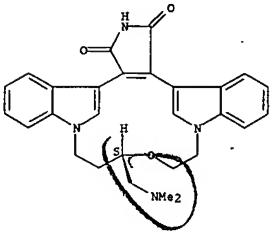
RN 169939-93-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 43 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

CRN 169939-94-0
CMF C28 H28 N4 O3

Absolute stereochemistry.

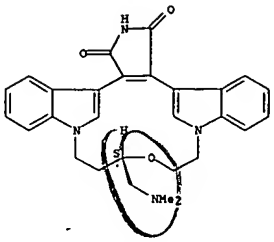


CM 2

CRN 75-75-2
CMF C H4 O3 S

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

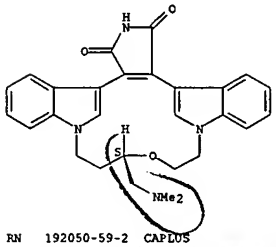
L54 ANSWER 43 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



● HCl

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 192050-59-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (S)-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

L54 ANSWER 44 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:161132 CAPLUS
DOCUMENT NUMBER: 128:221637
TITLE: Use of protein kinase C inhibitors for the manufacture of a medicament for the treatment of AIDS
INVENTOR(S): Jirousek, Michael R.; Ways, Douglas K.; Stramm, Lawrence E.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9808509	A1	19980305	WO 1997-US15525	19970828
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6107327	A	20000822	US 1997-917033	19970826
AU 9741794	A1	19980319	AU 1997-41794	19970828
BR 9711329	A	19990817	BR 1997-11329	19970828
CN 1228696	A	19990915	CN 1997-197537	19970828
EP 830860	A1	19980325	EP 1997-306714	19970901
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 9900949	A	19990226	NO 1999-949	19990226
KR 2000035861	A	20000626	KR 1999-7001556	19990226

PRIORITY APPLN. INFO.: US 1996-24873P P 19960830
US 1997-917033 A 19970826
US 1996-24873 A 19960830
WO 1997-US15525 W 19970828

OTHER SOURCE(S): MARPAT 128:221637

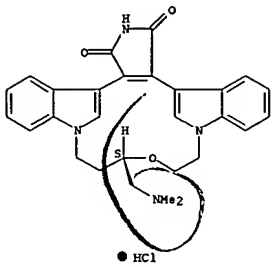
AB A method for treating HIV infection is disclosed, particularly using the isoenzyme selective PKC inhibitor, (S)-3,4-[N,N'-1,1'-((2''-ethoxy)-3'''(O)-4'''-(N,N-dimethylamino)-butane)-bis(3,3'-indolyl)]-1(H)-pyrrole-2,5-dione or its acid salt. Capsule and tablet formulations are given.

IT 169939-93-9 169939-94-0 192050-59-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein kinase C inhibitors for pharmaceuticals for the treatment of AIDS)

RN 169939-93-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

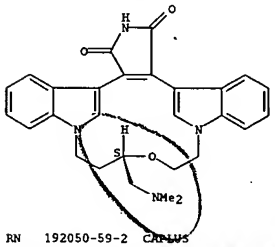
L54 ANSWER 44 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



● HCl

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



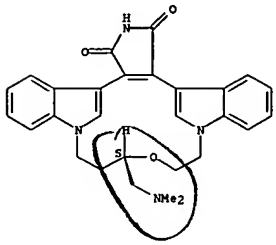
RN 192050-59-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (S)-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

L54 ANSWER 44 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

CRN 169939-94-0
CMF C28 H28 N4 O3

Absolute stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 45 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1998:161131 CAPLUS
DOCUMENT NUMBER: 128:221636
TITLE: Use of protein kinase C inhibitors for the manufacture of a medicament for the treatment of HTLV-1 infections
INVENTOR(S): Jirousek, Michael R.; Ways, Douglas K.; Stramm, Lawrence E.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9808508	A1	19980305	WO 1997-US15524	19970828
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5962446	A	19991005	US 1997-917517	19970826
AU 9741793	A1	19980319	AU 1997-41793	19970828
BR 9711366	A	19990817	BR 1997-11366	19970828
CN 1231608	A	19991013	CN 1997-198160	19970828
EP 830861	A1	19980325	EP 1997-306715	19970901
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 9900948	A	19990428	NO 1999-948	19990226
KR 2000035864	A	20000626	KR 1999-7001559	19990226

PRIORITY APPLN. INFO.: US 1996-24938P P 19960830
US 1997-917517 A 19970826
US 1996-24938 A 19960830
WO 1997-US15524 W 19970828

OTHER SOURCE(S): MARPAT 128:221636

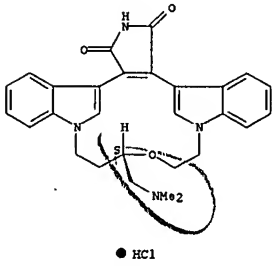
AB A method for treating human T cell lymphotrophic virus type 1 infection using an isoenzyme selective PKC inhibitor, particularly using the isoenzyme selective PKC inhibitor, (S)-3,4-[N,-N'-1,1'-{(2''-ethoxy)-3'''(O)-4'''-(N,N-dimethylamino)butane}-bis(3,3'-indolyl)]-1(H)-pyrrole-2,5-dione hydrochloride. Pharmaceutical formulations are given.

IT 169939-93-9 169939-94-0 192050-59-2
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein kinase C inhibitors for the manuf. of a medicament for the treatment of HTLV-1 infections)

RN 169939-93-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

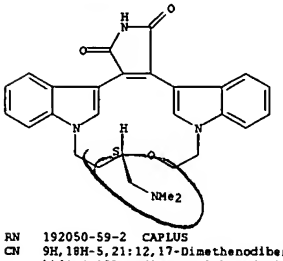
L54 ANSWER 45 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



● HCl

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



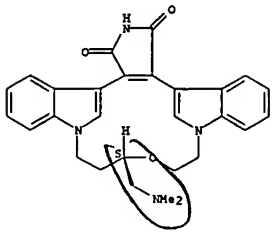
RN 192050-59-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (S)-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 169939-94-0
CMF C28 H28 N4 O3

Absolute stereochemistry.

L54 ANSWER 45 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

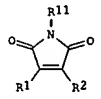


CM 2

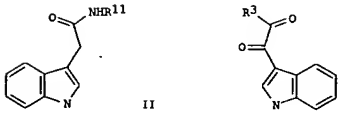
CRN 75-75-2
CMF C H4 O3 S

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 46 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



I



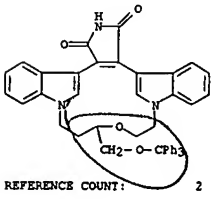
II III

AB The title compds. [I; R1, R2 = (un)substituted 3-indolyl; R11 = H, Me], useful as potent PKC inhibitors, were prepd. by reaction of optionally substituted indole-3-acetamide II with optionally substituted indole-3-glyoxyl reagent III [R3 = I, Cl, Br, OR4; R4 = C1-4 alkyl] in the presence of a base sufficiently strong to deprotonate the amide and methylene at the C-3 position of the indolyl-3-acetamide II. The reaction is very efficient and robust macrocyclization methodol. Compds. I are effective at 0.1-5 mg/kg/day.

IT **203719-63-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of bisindolylmaleimides as potent PKC inhibitors)

RN 203719-63-5 CAPLUS

CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[(triphenylmethoxy)methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 46 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1998:147304 CAPLUS
DOCUMENT NUMBER: 128:192545
TITLE: Synthesis of bisindolylmaleimides as potent PKC inhibitors
INVENTOR(S): Faul, Margaret Mary; Winneroski, Leonard L., Jr.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9807693	A1	19980226	WO 1997-US14771	19970822
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
EP 825190	A1	19980225	EP 1997-306438	19970822
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, RO				
AU 9741570	A1	19980306	AU 1997-41570	19970822
AU 716840	B2	20000309		
BR 9711363	A	19990817	BR 1997-11363	19970822
CN 1228082	A	19990908	CN 1997-197361	19970822
US 5990319	A	19991123	US 1997-917052	19970822
NZ 334030	A	20000825	NZ 1997-334030	19970822
JP 2000516632	T2	20001212	JP 1998-510991	19970822
US 5948907	A	19990907	US 1998-81252	19980519
US 6133452	A	20001017	US 1999-234722	19990121
NO 9900832	A	19990413	NO 1999-832	19990222

PRIORITY APPLN. INFO.: US 1996-24120P P 19960823
US 1997-917052 A 19970822
WO 1997-US14771 W 19970822
OTHER SOURCE(S): CASREACT 128:192545; MARPAT 128:192545
GI

L54 ANSWER 47 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1998:147201 CAPLUS
DOCUMENT NUMBER: 128:208919
TITLE: Therapeutic treatment for sexual dysfunctions
INVENTOR(S): Jirousek, Michael R.; Ways, Douglas Kirk; Stramm, Lawrence E.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9807422	A1	19980226	WO 1997-US14795	19970822
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6093709	A	20000725	US 1997-915303	19970819
AU 9741575	A1	19980306	AU 1997-41575	19970822
AU 731260	B2	20010329		
EP 829262	A2	19980318	EP 1997-306425	19970822
EP 829262	A3	19980325		
EP 829262	B1	20011219		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9711210	A	19990817	BR 1997-11210	19970822
JP 2001500478	T2	20010116	JP 1998-511002	19970822
AT 210981	E	20020115	AT 1997-306425	19970822
ES 2122953	T3	20020701	ES 1997-306425	19970822
NO 9900794	A	19990421	NO 1999-794	19990219

PRIORITY APPLN. INFO.: US 1996-23425P P 19960822
US 1997-915303 A 19970819
WO 1997-US14795 W 19970822
OTHER SOURCE(S): MARPAT 128:208919

AB A method for treating sexual dysfunctions is disclosed, particularly using the isoenzyme selective PKC inhibitor, (S)-3,4-[N,N'-1,1'-[(2''-ethoxy)-3'''(O)-4'''-(N,N-dimethylamino)-butane]-bis-(3,3'-indolyl)]-1(H)-pyrrole-2,5-dione, particularly its hydrochloride, or mesylate salt. Formulations for tablets and capsules contg. the active ingredients are provided.

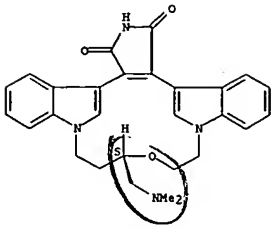
IT **169939-93-9 169939-94-0 192050-59-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bis-indolylmaleimides for treatment of sexual dysfunctions)

RN 169939-93-9 CAPLUS

CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

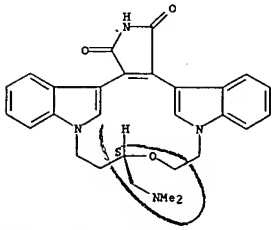
L54 ANSWER 47 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



● HCl

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 192050-59-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-{(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (S)-, monomethanesulfonate (9CI) (CA INDEX NAME)

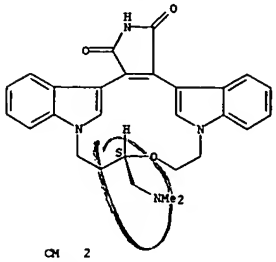
CM 1

CRN 169939-94-0

L54 ANSWER 47 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

CMF C28 H28 N4 O3

Absolute stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S

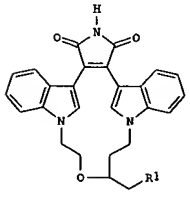
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 48 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1998:146703 CAPLUS
DOCUMENT NUMBER: 128:192679
TITLE: Preparation of N,N'-oxalkylene-bridged bis(indolyl)maleimides as protein kinase C inhibitors
INVENTOR(S): Faul, Margaret Mary; Krumrich, Christine Ann; Winneroski, Leonard Larry, Jr.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 12 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5721272	A	19980224	US 1996-749608	19961118

PRIORITY APPLN. INFO.: US 1996-749608 19961118
OTHER SOURCE(S): CASREACT 128:192679; MARPAT 128:192679
GI

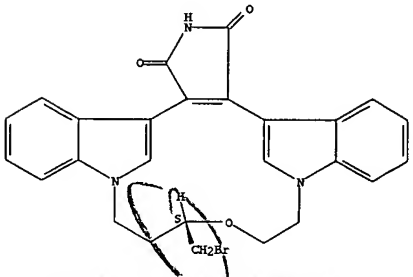


I

AB Title compds. (I; R1 = Br,iodo, OSO2C6H4Me-4) were prepd. as intermediates for the corresponding amines and tested for protein kinase C inhibitory activity (data given).
IT 191848-29-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of N,N'-oxalkylene-bridged bis(indolyl)maleimides as protein kinase C inhibitors)
RN 191848-29-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-(bromomethyl)-6,7,10,11-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

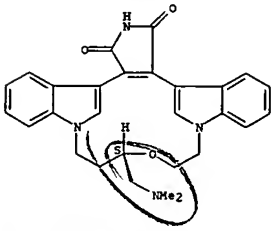
Absolute stereochemistry.

L54 ANSWER 48 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



IT 169939-94-0P 178687-81-5P 191848-30-3P
191848-31-4P 191848-32-5P 191848-33-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N,N'-oxalkylene-bridged bis(indolyl)maleimides as protein kinase C inhibitors)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-{(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

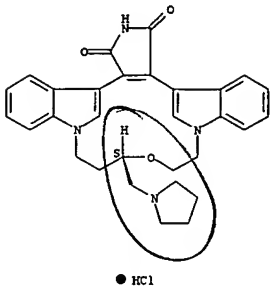
Absolute stereochemistry.



RN 178687-81-5 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(1-pyrrolidinylmethyl)-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

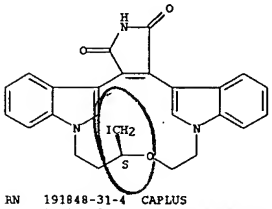
L54 ANSWER 48 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



● HCl

RN 191848-30-3 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(iodomethyl)-, (S)- (9CI) (CA INDEX NAME)

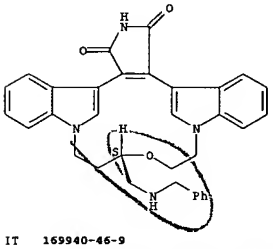
Absolute stereochemistry.



RN 191848-31-4 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[(4-methylphenyl)sulfonyl]oxy]-, (S)- (9CI) (CA INDEX NAME)

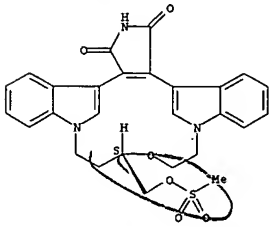
Absolute stereochemistry.

L54 ANSWER 48 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



IT 169940-46-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of N,N'-oxalkylene-bridged bis(indolyl)maleimides as protein kinase C inhibitors)
RN 169940-46-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[(methylsulfonyl)oxy]methyl]-, (S)- (9CI) (CA INDEX NAME)

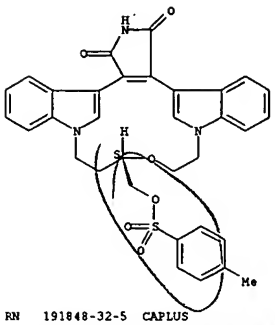
Absolute stereochemistry.



IT 169940-55-0P 170277-74-4P 170277-76-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of N,N'-oxalkylene-bridged bis(indolyl)maleimides as protein kinase C inhibitors)
RN 169940-55-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(hydroxymethyl)-, (S)- (9CI) (CA INDEX NAME)

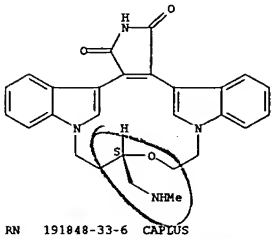
Absolute stereochemistry.

L54 ANSWER 48 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 191848-32-5 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[(methylamino)methyl]-, (9S)- (9CI) (CA INDEX NAME)

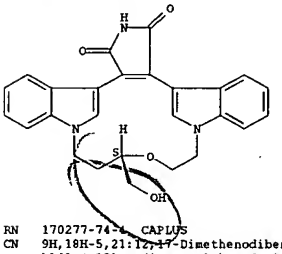
Absolute stereochemistry.



RN 191848-33-6 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[(phenylmethyl)amino]methyl]-, (S)- (9CI) (CA INDEX NAME)

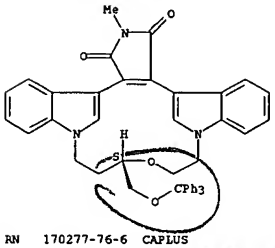
Absolute stereochemistry.

L54 ANSWER 48 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 170277-74-4 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-19-methyl-9-[(triphenylmethoxy)methyl]-, (S)- (9CI) (CA INDEX NAME)

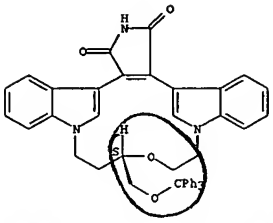
Absolute stereochemistry.



RN 170277-76-6 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[(triphenylmethoxy)methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

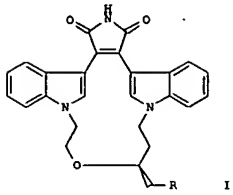
L54 ANSWER 48 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 49 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1998:136147 CAPLUS
DOCUMENT NUMBER: 128:192635
TITLE: Macrocyclic Bisindolylmaleimides: Synthesis by Inter- and Intramolecular Cyclization
AUTHOR(S): Faul, Margaret M.; Winneroski, Leonard L.; Krumrich, Christine A.; Sullivan, Kevin A.; Gillig, James R.; Neel, David A.; Rito, Christopher J.; Jirousek, Michael R.
CORPORATE SOURCE: Lilly Research Laboratories Chemical Process Research and Development Division, Eli Lilly and Company, Indianapolis, IN, 46285-4813, USA
SOURCE: Journal of Organic Chemistry (1998), 63(6), 1961-1973
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



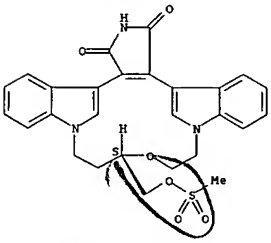
AB Macrocyclic bisindolylmaleimides I (R = NMe2, 1-pyrrolidinyl, NHCH2Ph, NHMe) have been identified as competitive reversible inhibitors of PKC .beta.1 and .beta.2 and are being advanced to the clinic for evaluation as a treatment of retinopathy assocd. with diabetic complications. Highly convergent and stereoselective syntheses of I have been developed. The key synthetic step involves intermol. cyclization of a bisalkylating agent, (S)-3-[2-[(methylsulfonyl)oxy]ethoxy]-4-(triphenylmethoxy)-1-butanol methanesulfonate, with sym. bisindolylmaleimide that is amenable to the prepn. of multikilogram quantities of these compds. The synthetic sequence to I (R = NMe2), the most active compd., proceeds in 11 steps and 26% overall yield (>98% ee) from (R)-1-chloro-2,3-propanediol. No chromatog. purifns. are required throughout the process, and the final product is isolated in >97% purity after crystn. from DMF/MeOH. Synthesis of I by intramol. cyclization proved less efficient, requiring 17 steps and affording I in lower overall yields of 6.0-8.5%.

IT 169940-46-9P 169940-55-0P 170277-74-4P
170277-76-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

L54 ANSWER 49 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
(macrocyclic bisindolylmaleimides via inter- and intramol. cyclization)

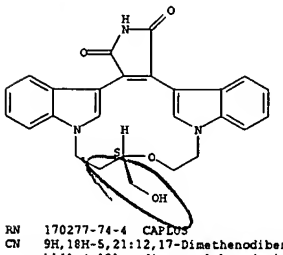
RN 169940-46-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[(methylsulfonyl)oxy]methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 169940-55-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(hydroxymethyl)-, (S)- (9CI) (CA INDEX NAME)

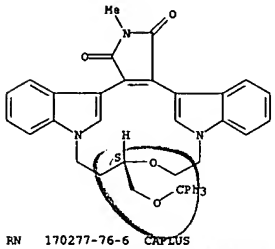
Absolute stereochemistry.



RN 170277-74-4 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-19-methyl-9-[(triphenylmethoxy)methyl]-, (S)- (9CI) (CA INDEX NAME)

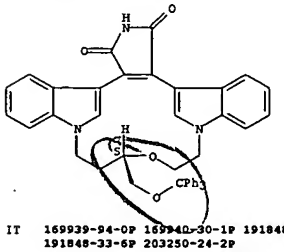
Absolute stereochemistry.

L54 ANSWER 49 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 170277-76-6 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[(triphenylmethoxy)methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

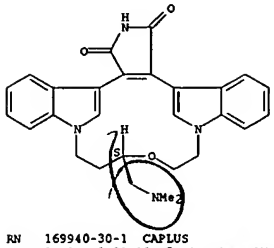


IT 169939-94-0P 169940-30-1P 191848-32-5P
191848-33-6P 203250-24-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(macrocyclic bisindolylmaleimides via inter- and intramol. cyclization)

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

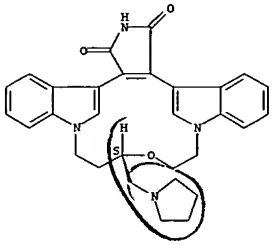
Absolute stereochemistry.

L54 ANSWER 49 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 169940-30-1 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(1-pyrrolidinylmethyl)-, (S)- (9CI) (CA INDEX NAME)

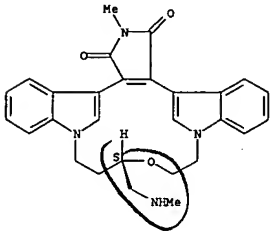
Absolute stereochemistry.



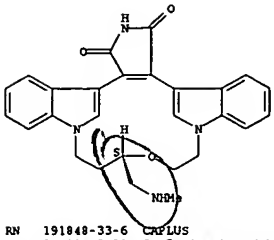
RN 191848-32-5 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[(methylamino)methyl]-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 49 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

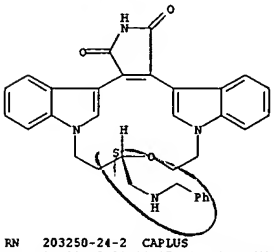


L54 ANSWER 49 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 191848-33-6 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[(phenylmethyl)amino]methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 203250-24-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-19-methyl-9-[(methylamino)methyl]-, (S)- (9CI) (CA INDEX NAME)

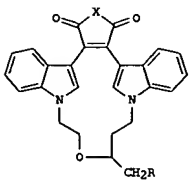
Absolute stereochemistry.

L54 ANSWER 50 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:62223 CAPLUS
DOCUMENT NUMBER: 128:140735
TITLE: Preparation of bis-indolylmaleimide macrocycle derivative as protein kinase C inhibitor
INVENTOR(S): Engel, Gary Lowell; Farid, Nagy Alphonse; Faul, Margaret Mary; Jirousek, Michael Robert; Richardson, Lori Ann; Winneroski, Leonard Larry, Jr.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 12 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5710145	A	19980120	US 1996-749607	19961118
US 6015807	A	20000118	US 1997-966081	19971107
US 6117861	A	20000912	US 1999-455697	19991207

PRIORITY APPLN. INFO.: US 1995-6970P P 19951120
US 1996-749607 A1 19961118
US 1997-966081 A1 19971107

GI



I

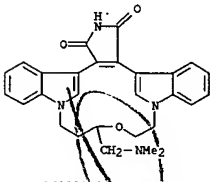
AB This invention provides novel bis-indolylmaleimide macrocycle derivs. of the formula (I.MeSO3H; X = NH, R = NMe2) and solvates thereof, in particular (S)-I.MeSO3H (X = NH, R = NMe2), namely (S)-13-[(dimethylamino)methyl]-10,11,14,15-tetrahydro-4,9:16,21-dimetheno-1H,13H-dibenzo[E,K]pyrrolo[3,4-H][1,4,13]-oxadiazacyclohexadecine-1,3(2H)-dione methanesulfonate monohydrate. The invention further provides the prepn., pharmaceutical formulations and the methods of use for inhibiting protein kinase c in mammals. A method of treating microvascular diabetic complications comprises administering to a mammal in need thereof, a pharmaceutically effective amt. of a compd. of I.MeSO3H (X = NH, R = NMe). Most unexpectedly, the claimed mesylate salt form has improved soly. and dramatically improved bioavailability to the patient and furthermore, is readily prepd. and purified as a cryst. form. Thereby, it is more pharmaceutically elegant and a much improved therapeutic agent and is useful in treating conditions assocd. with diabetes mellitus and its complications, ischemia, inflammation, central nervous system disorders, cardiovascular disease, dermatol. disease, and cancer (no data). Thus,

L54 ANSWER 50 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
2,3-bis(1H-indol-3-yl)-N-methylmaleimide was cyclocondensed with (S)-3-[2-(methanesulfonyloxy)ethoxy]-4-trityloxy-1-(methanesulfonyloxy)butane methanesulfonate in the presence of Cesium carbonate in DMF at 50.degree. for 70-72 h to give 89% (S)-I (X = NMe, R = OCPh3) which was suspended in EtOH and 10 N aq. KOH, heated to a gentle reflux, and acidified with aq. 10N HCl to give 80% (S)-I (X = O, R = OCPh3). The latter compd. was dissolved in DMF, treated with a premixed soln. of MeOH and 1,1,1,3,3,3-hexamethyldisilazane, and heated at 45.degree. for 7 h to give 100% (S)-I (X = NH, R = OCPh3), which was detritylated with HCl in CH2Cl2 to give 90% (S)-I (X = NH, R = OH) and then mesylated by methanesulfonic anhydride in pyridine and THF to give 81% (S)-I (X = NH, R = OSO2Me). This was heated with a mixt. of 40% aq. Me2NH and THF at 65.degree. in a sealed reactor for 19 h to give 91% (S)-I (X = NH, R = NMe2), which was converted into the mesylate salt (S)-I.MeSO3H (X = NH, R = NMe2). The soly. of the mesylate salt in water was 1,760 .mu.g/mL compared to 0.5, 1, 14, 71, 268, and 736 .mu.g/mL for the succinate, acetate, sulfate, hydrochloride, and phosphate salt of (S)-I (X = NH, R = NMe2). It showed greater than 1.5 times the bioavailability of the HCl salt when administered p.o. to dogs. Formulations such as hard gelatin capsules, tablet, and capsules contg. I.MeSO3H were described.

IT **169939-91-7P 169939-93-9P 169939-94-0P**
191937-15-2P 192050-59-2P 202260-21-7P
202260-22-8P 202260-23-9P 202260-24-0P
202260-25-1P 202260-26-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of bis-indolylmaleimide macrocycle deriv. as protein kinase C inhibitor for treatment of diseases)

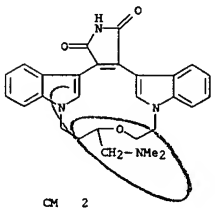
RN 169939-91-7 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro- (9CI) (CA INDEX NAME)



RN 169939-93-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, (9S)- (9CI) (CA INDEX NAME)

L54 ANSWER 50 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

CRN 169939-91-7
CMF C28 H28 N4 O3



CM 2

CRN 75-75-2
CMF C H4 O3 S

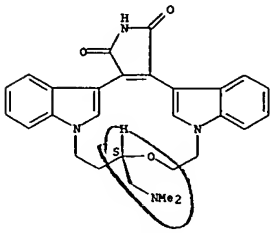
RN 192050-59-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (S)-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 169939-94-0
CMF C28 H28 N4 O3

Absolute stereochemistry.

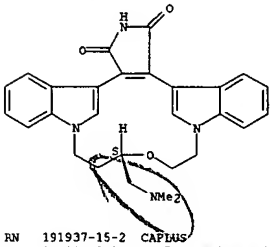
L54 ANSWER 50 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
Absolute stereochemistry.



● HCl

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

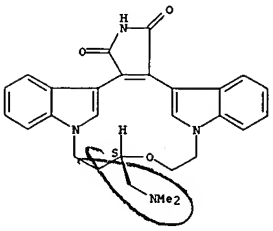
Absolute stereochemistry.



RN 191937-15-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

L54 ANSWER 50 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



CM 2

CRN 75-75-2
CMF C H4 O3 S

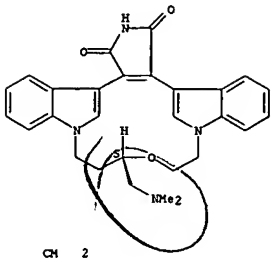
RN 202260-21-7 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)-, monomethanesulfonate, monohydrate (9CI) (CA INDEX NAME)

CM 1

CRN 169939-94-0
CMF C28 H28 N4 O3

Absolute stereochemistry.

L54 ANSWER 50 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



CM 2

CRN 75-75-2
CMF C H4 O3 S

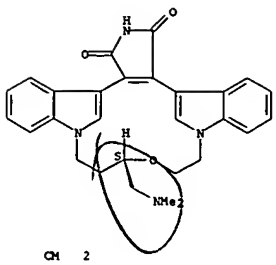
RN 202260-22-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (S)-, sulfate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 169939-94-0
CMF C28 H28 N4 O3

Absolute stereochemistry.

L54 ANSWER 50 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



CM 2

CRN 7664-93-9
CMF H2 O4 S

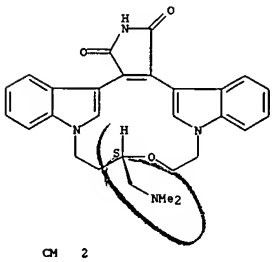
RN 202260-23-9 CAPLUS
CN Butanedioic acid, compd. with (S)-9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-9H,18H-5,21:12,17-dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 169939-94-0
CMF C28 H28 N4 O3

Absolute stereochemistry.

L54 ANSWER 50 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



CM 2

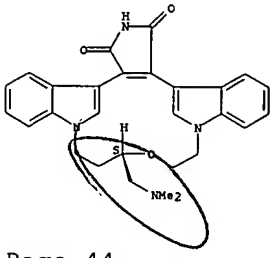
CRN 110-15-6
CMF C4 H6 O4

RN 202260-24-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (S)-, monoacetate (9CI) (CA INDEX NAME)

CM 1

CRN 169939-94-0
CMF C28 H28 N4 O3

Absolute stereochemistry.



L54 ANSWER 50 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

CM 2

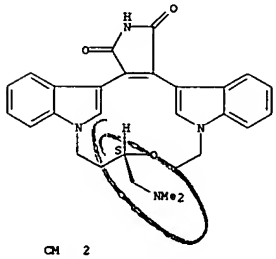
CRN 64-19-7
CMF C2 H4 O2

RN 202260-25-1 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (S)-, phosphate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 169939-94-0
CMF C28 H28 N4 O3

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

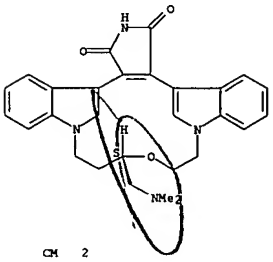
RN 202260-26-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (S)-, (2R,3R)-2,3-

L54 ANSWER 50 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 169939-94-0
CMF C28 H28 N4 O3

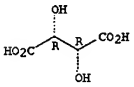
Absolute stereochemistry.



CM 2

CRN 87-69-4
CMF C4 H6 O6

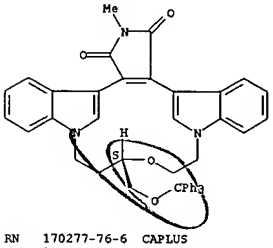
Absolute stereochemistry.



IT 169940-46-9P 169940-55-0P 170277-74-4P
170277-76-6P 202002-90-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of bis-indolylmaleimide macrocycle deriv. as protein kinase C inhibitor for treatment of diseases)
RN 169940-46-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[(methylsulfonyl)oxy]methyl]-, (S)- (9CI) (CA INDEX NAME)

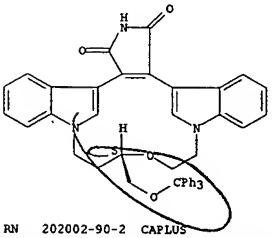
Absolute stereochemistry.

L54 ANSWER 50 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 170277-76-6 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[(triphenylmethoxy)methyl]-, (S)- (9CI) (CA INDEX NAME)

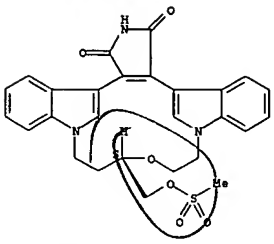
Absolute stereochemistry.



RN 202002-90-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-6,7,10,11-tetrahydro-19-methyl-, (S)- (9CI) (CA INDEX NAME)

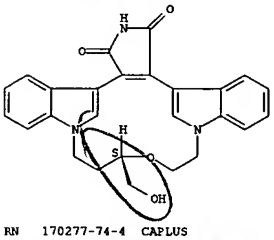
Absolute stereochemistry.

L54 ANSWER 50 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 169940-55-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(hydroxymethyl)-, (S)- (9CI) (CA INDEX NAME)

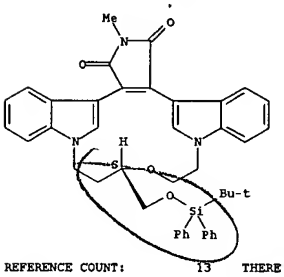
Absolute stereochemistry.



RN 170277-74-4 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-19-methyl-9-[(triphenylmethoxy)methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 50 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 51 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:29884 CAPLUS
DOCUMENT NUMBER: 128:178752
TITLE: Inhibition of telomerase activity by PKC inhibitors in human nasopharyngeal cancer cells in culture
AUTHOR(S): Ku, Wei-Chi; Cheng, Ann-Joy; Wang, Tzu-Chien V.
CORPORATE SOURCE: Department of Molecular and Cellular Biology, College of Medicine, Chang Gung University, Kwei-San, Taiwan
SOURCE: Biochemical and Biophysical Research Communications (1997), 241(3), 730-736
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

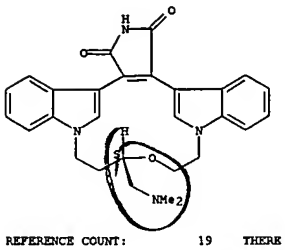
AB Telomerase is a specialized ribonucleoprotein polymerase that adds hexanucleotides (TTAGGG) onto human chromosomal ends. The expression of telomerase activity has been assocd. with cell immortalization and the malignant phenotype in most cancers. How the telomerase activity is regulated in cancer cells is presently not known. In this work, the effects of cell cycle blockers, DNA damaging agents, TopII inhibitors and proteins kinase inhibitors on the telomerase activity were examd. in cultured nasopharyngeal carcinoma cells NPC-076. Agents which interfere with tubulin assembly (Taxol and vinblastine) and agents which arrest cells at S phase (methotrexate and 5-fluorouracil) did not inhibit telomerase activity of treated cells. Agents which damage DNA (cisplatin, Me methanesulfonate, and UV radiation) and TopII inhibitors (etoposide and daunorubicin) also did not inhibit telomerase activity of treated cells. Among the protein kinase inhibitors examd., no significant inhibition of telomerase activity was obsd. with cells treated with quercetin, H-89, or herbimycin A. On the other hand, two protein kinase C (PKC) inhibitors (bisindolylmaleimide I and H-7) were found to produce a big inhibition of telomerase activity in treated cells. Staurosporine produced a moderate inhibition, and sphingosine had a small inhibitory effect. The inhibition of telomerase activity by PKC inhibitors appears to be specific since the treated cells were mostly viable (i.e., greater than 75%) and still retained significant levels of protein synthesis capability. These results implicate that protein kinase C is involved in the regulation of telomerase activity in vivo.

IT 169939-94-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of telomerase activity by PKC inhibitors in human nasopharyngeal cancer cells)

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 51 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L54 ANSWER 52 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:13840 CAPLUS
DOCUMENT NUMBER: 128:84396
TITLE: Therapeutic treatment for cardiovascular diseases using protein kinase C inhibitors
INVENTOR(S): Jirousek, Michael R.; Heath, William Francis, Jr.; Ways, Douglas Kirk; Stramm, Lawrence E.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA; Jirousek, Michael R.; Heath, William Francis, Jr.; Ways, Douglas Kirk; Stramm, Lawrence E.
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9747298	A1	19971218	WO 1997-US9661	19970612
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5723456	A	19980303	US 1996-662623	19960613
AU 9734763	A1	19980107	AU 1997-34763	19970612
AU 725582	B2	20001012		
CN 1225012	A	19990804	CN 1997-196421	19970612
BR 9709727	A	19990810	BR 1997-9727	19970612
EP 954308	A1	19991110	EP 1997-931034	19970612
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NZ 333341	A	20000526	NZ 1997-333341	19970612
JP 2000512293	T2	20000919	JP 1998-501674	19970612
NO 9805808	A	19990212	NO 1998-5808	19981211

PRIORITY APPLN. INFO.:
US 1996-662623 A1 19960613
US 1993-163060 B2 19931207
US 1994-316973 B2 19941003
US 1995-413735 A3 19950330
US 1996-643706 A2 19960506
WO 1997-US9661 W 19970612

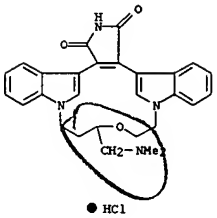
OTHER SOURCE(S): MARPAT 128:84396

AB A method for treating endothelial cell dysfunction, such as assocd. with cardiovascular disease, is disclosed, particularly using the isoenzyme selective PKC inhibitor, e.g. (S)-3,4-[N,N'-1,1'-((27''-ethoxy)-3''(O)-4'''-(N,N-dimethylamino)-butane)-bis-(3,3'-indolyl)]-1(H)-pyrrole-2,5-dione hydrochloride salt. Active-agent formulations are included.

IT 169939-90-6 169939-91-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein kinase C inhibitors for cardiovascular disease treatment)

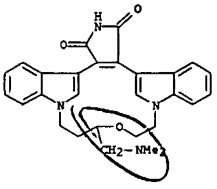
RN 169939-90-6 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride (9CI)

L54 ANSWER 52 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
(CA INDEX NAME)



● HCl

RN 169939-91-7 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro- (9CI) (CA INDEX NAME)



L54 ANSWER 53 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:740123 CAPLUS
DOCUMENT NUMBER: 128:10311
TITLE: Use of protein kinase C inhibitors to enhance the clinical efficacy of oncolytic agents and radiation therapy
INVENTOR(S): Jirousek, Michael R.; Stramm, Lawrence E.; Ways, Douglas Kirk
PATENT ASSIGNEE(S): Eli Lilly and Company, USA; Jirousek, Michael R.; Stramm, Lawrence E.; Ways, Douglas Kirk
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9740842	A1	19971106	WO 1997-US7801	19970501
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6232299	B1	20010515	US 1997-841738	19970430
AU 9730002	A1	19971119	AU 1997-30002	19970501
AU 718098	B2	20000406		
EP 914135	A1	19990512	EP 1997-924623	19970501
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1222850	A	19990714	CN 1997-195699	19970501
BR 9710704	A	19990817	BR 1997-10704	19970501
JP 2000510828	T2	20000822	JP 1997-539299	19970501
NZ 332563	A	20000825	NZ 1997-332563	19970501
NZ 504136	A	20020301	NZ 1997-504136	19970501
NO 9805065	A	19981228	NO 1998-5065	19981030
US 6288053	B1	20010911	US 1998-193713	19981117
US 2001001791	A1	20010524	US 2001-758020	20010110
US 6486179	B2	20021126		

PRIORITY APPLN. INFO.: US 1996-16658P P 19960501
US 1997-841738 A 19970430
NZ 1997-332563 A1 19970501
WO 1997-US7801 W 19970501

OTHER SOURCE(S): MARPAT 128:10311

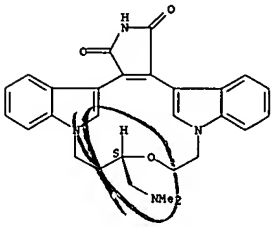
AB A method for treating neoplasms is disclosed, particularly using the .beta.-isoenzyme selective PKC inhibitor, (S)-3,4-[N,N'-1,1'-[(2''-ethoxy)-3'''(O)-4'''-(N,N-dimethylamino)-butane]-bis-(3,3'-indolyl)]-1(H)-pyrrole-2,5-dione or one of its salts, such PKC inhibitors enhance the clin. efficacy of oncolytic agents and radiation therapy.

IT 169939-94-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

L54 ANSWER 53 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
(Uses)
(protein kinase C inhibitors to enhance clin. efficacy of oncolytic agents and radiation therapy)

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L54 ANSWER 54 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:740114 CAPLUS
DOCUMENT NUMBER: 128:10324
TITLE: Bis(indolylmaleimide) compounds for treatment of VEGF-related ocular diseases
INVENTOR(S): Aiello, Lloyd P.; Jirousek, Michael R.; King, George L.; Vignati, Louis; Ways, Douglas Kirk
PATENT ASSIGNEE(S): Eli Lilly and Company, USA; Aiello, Lloyd P.; Jirousek, Michael R.; King, George L.; Vignati, Louis; Ways, Douglas Kirk
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9740831	A1	19971106	WO 1997-US7800	19970501
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6114320	A	20000905	US 1997-841739	19970430
AU 9729361	A1	19971119	AU 1997-29361	19970501
AU 724923	B2	20001005		
EP 918519	A1	19990602	EP 1997-923594	19970501
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1222850	A	19990714	CN 1997-195699	19970501
BR 9710705	A	19990817	BR 1997-10705	19970501
NZ 332833	A	20000728	NZ 1997-332833	19970501
JP 2000514402	T2	20001031	JP 1997-539298	19970501
NZ 504136	A	20020301	NZ 1997-504136	19970501
NO 9805067	A	19981222	NO 1998-5067	19981030
MX 9809160	A	20000531	MX 1998-9160	19981103

PRIORITY APPLN. INFO.: US 1996-16658P P 19960501
US 1997-841739 A 19970430
US 1997-841738 A 19970430
NZ 1997-332563 A1 19970501
WO 1997-US7800 W 19970501

OTHER SOURCE(S): MARPAT 128:10324

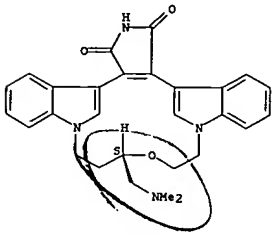
AB A method for inhibiting VEGF-stimulated endothelial cell growth, such as assocd. with macular degeneration, and VEGF-stimulated capillary permeability, such as assocd. with macular edema are disclosed, particularly using the isoenzyme selective PKC inhibitor, (S)-3,4-[N,N'-1,1'-[(2''-ethoxy)-3'''(O)-4'''-(N,N-dimethylamino)-butane]-bis-(3,3'-indolyl)]-1(H)-pyrrole-2,5-dione.cntdot.HCl (I). I at 0.1-100 nM significantly inhibited growth factor-stimulated nonbasal cell growth in vitro.

IT 169939-93-9 169939-94-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein kinase C .beta.-isoenzyme inhibitors for treatment of

L54 ANSWER 54 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
VEGF-related ocular diseases)

RN 169939-93-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, (9S)- (9CI) (CA INDEX NAME)

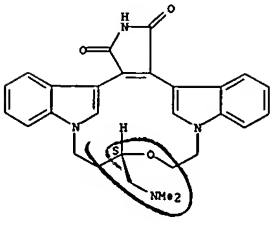
Absolute stereochemistry.



● HCl

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L54 ANSWER 55 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:740113 CAPLUS
DOCUMENT NUMBER: 128:10310
TITLE: Therapeutic treatment for VEGF-related diseases
INVENTOR(S): Jirousek, Michael R.; Vignati, Louis; Ways, Douglas Kirk
PATENT ASSIGNEE(S): Eli Lilly and Company, USA; Jirousek, Michael R.; Vignati, Louis; Ways, Douglas Kirk
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9740830	A1	19971106	WO 1997-US7752	19970501
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9729355	A1	19971119	AU 1997-29355	19970501
AU 736333	B2	20010726		
EP 915698	A1	19990519	EP 1997-923587	19970501
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1222850	A	19990714	CN 1997-195699	19970501
BR 9710706	A	19990817	BR 1997-10706	19970501
CN 1233177	A	19991027	CN 1997-196010	19970501
NZ 332645	A	20000728	NZ 1997-332645	19970501
JP 2002504086	T2	20020205	JP 1997-539293	19970501
NZ 504136	A	20020301	NZ 1997-504136	19970501
NO 9805066	A	19981221	NO 1998-5066	19981030
US 6284751	B1	20010904	US 1999-335887	19990618

PRIORITY APPLN. INFO.: US 1996-16658P P 19960501
US 1997-841635 A 19970430
US 1997-841738 A 19970430
NZ 1997-332563 A1 19970501
WO 1997-US7752 W 19970501

OTHER SOURCE(S): MARPAT 128:10310

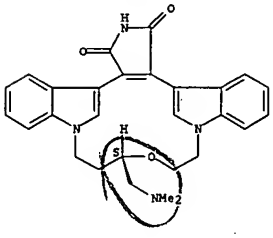
AB A method for inhibiting VEGF-stimulated endothelial cell growth, such as assocd. with neoplasia, and VEGF-stimulated capillary permeability, such as assocd. with pulmonary edema are disclosed, particularly using the .beta.-isoenzyme selective PKC inhibitor, (S)-3,4-[N,N'-1,1'-[(2''-ethoxy)-3'''(0)-4'''-(N,N-dimethylamino)-butane]-bis-(3,3'-indolyl)]-1(H)-pyrrole-2,5-dione hydrochloride salt.

IT 169939-93-9 169939-94-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bis(indolylmaleimide) compds. for treatment of VEGF-related diseases)

L54 ANSWER 55 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

L54 ANSWER 55 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
RN 169939-93-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, (9S)-(9CI) (CA INDEX NAME)

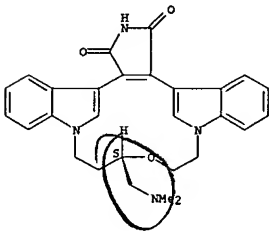
Absolute stereochemistry.



● HCl

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L54 ANSWER 56 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:732137 CAPLUS
DOCUMENT NUMBER: 128:13371
TITLE: Preparation of halo-substituted bis-indolemaleimides as protein kinase C inhibitors
INVENTOR(S): Goekjian, Peter G.; Jirousek, Michael R.; Wu, Guo-zhang
PATENT ASSIGNEE(S): Mississippi State University, USA; Eli Lilly and Company
SOURCE: Eur. Pat. Appl., 61 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 805158	A2	19971105	EP 1997-302996	19970501
EP 805158	A3	19980401		
EP 805158	B1	20020116		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
WO 9741127	A1	19971106	WO 1997-US7302	19970430
W: AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, FI, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RU, SD, SG, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9729292	A1	19971119	AU 1997-29292	19970430
AU 703395	B2	19990325		
CN 1223658	A	19990721	CN 1997-195948	19970430
BR 9709301	A	19990810	BR 1997-9301	19970430
US 5936084	A	19990810	US 1997-846272	19970430
JP 11509233	T2	19990817	JP 1997-522343	19970430
JP 3235840	B2	20011204		
NZ 332658	A	20000526	NZ 1997-332658	19970430
AT 212026	E	20020215	AT 1997-302996	19970501
ES 2170918	T3	20020816	ES 1997-302996	19970501
NO 9805080	A	19981208	NO 1998-5080	19981030

PRIORITY APPLN. INFO.: US 1996-16382P P 19960501
WO 1997-US7302 W 19970430

OTHER SOURCE(S): MARPAT 128:13371
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

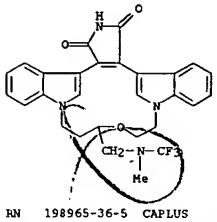
AB The present invention is directed to novel halo-substituted bis-indolemaleimide compds. I [R = H, halogen, OH, alkyl, alkoxy, NR3R4, acylamino; V = O, NH, N-alkyl; T, W = (un)substituted alkylene; J = XC(Y)(S); T = W = CH2, J = (CH2)nCH2C(CH2NR3R4):C(halogen), (CH2)nC(halogen):C(CH2NR3R4)(CH2)m, C(halogen):CHCH(CH2NR3R4)(CH2)n; m, n = 1, 2; X = O, S, bond; Y = halogen, H, alkyl; S = CHO, CZMR2; M = H, CH2OR5, CH2NR3R4, NR3R4; R2 = H, halogen; Z = H, OR6; R3, R4 = H, alkyl, haloalkyl, alkanoyl, haloalkanoyl; R3R4 = CR7R8; R7, R8 = H, alkyl, haloalkyl; CR7R8 = cyclopentayl cyclohexyl ring, when Y, S, T or W is a

L54 ANSWER 56 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

halogen or haloalkyl group or when T and W = methylene] and the prepn. of pharmaceutical formulations for use in inhibiting protein kinase C in mammals. Thus, staurosporine analog II was prepd. via condensation of N-methylbis(indol-3-yl)maleimide with dimesylate III. II showed protein kinase C inhibition [IC50 = 1300 nM (vs PKC.alpha.) and IC50 = 90 nM (vs PKC.beta.)].

IT **191848-45-0P 198965-36-5P 198965-42-3P**
198965-60-5P 198965-64-9P 199119-12-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of halo-substituted bis-indolemaleimides as protein kinase C inhibitors)

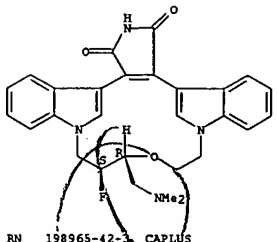
RN 191848-45-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[methyl(trifluoromethyl)amino]methyl]- (9CI) (CA INDEX NAME)



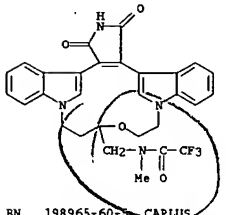
RN 198965-36-5 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-10-fluoro-6,7,10,11-tetrahydro-, (9R,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 56 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



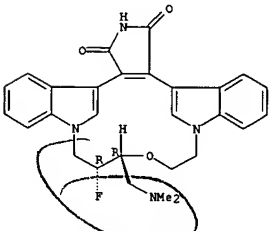
RN 198965-42-3 CAPLUS
CN Acetamide, 2,2,2-trifluoro-N-[(6,7,10,11,19,20-hexahydro-18,20-dioxo-9H,18H-5,21:12,17-dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecin-9-yl)methyl]-N-methyl- (9CI) (CA INDEX NAME)



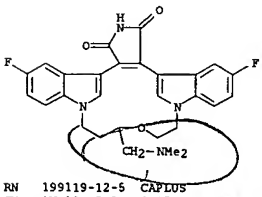
RN 198965-60-5 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-10-fluoro-6,7,10,11-tetrahydro-, (9R,10R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 56 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



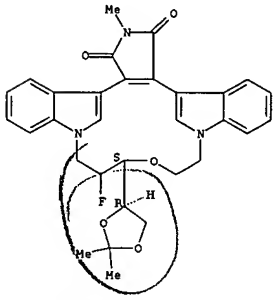
RN 198965-64-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-2,15-difluoro-6,7,10,11-tetrahydro- (9CI) (CA INDEX NAME)



RN 199119-12-5 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-(2,2-dimethyl-1,3-dioxolan-4-yl)-10-fluoro-6,7,10,11-tetrahydro-19-methyl-, [9S(R)]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

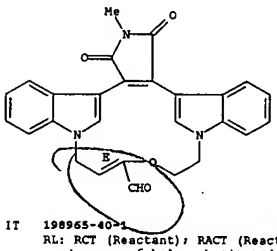
L54 ANSWER 56 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



IT **198965-51-4P**
RL: BYP (Byproduct); PREP (Preparation)
(prepn. of halo-substituted bis-indolemaleimides as protein kinase C inhibitors)

RN 198965-51-4 CAPLUS
CN 11H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-9-carboxaldehyde, 6,7,19,20-tetrahydro-19-methyl-18,20-dioxo-, (E)- (9CI) (CA INDEX NAME)

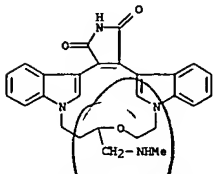
Double bond geometry as described by E or Z.



IT **198965-40-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of halo-substituted bis-indolemaleimides as protein kinase C inhibitors)

RN 198965-40-1 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[(methylamino)methyl]- (9CI) (CA INDEX NAME)

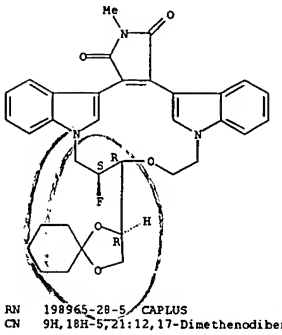
L54 ANSWER 56 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



IT 198965-27-4P 198965-28-5P 198965-30-9P
198965-32-1P 198965-33-2P 198965-34-3P
198965-39-8P 198965-41-2P 198965-56-9P
198965-57-0P 198965-58-1P 198965-59-2P
198965-62-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of halo-substituted bis-indolemaleimides as protein kinase C inhibitors)

RN 198965-27-4 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(2R)-1,4-dioxaspiro[4.5]dec-2-yl]-10-fluoro-6,7,10,11-tetrahydro-19-methyl-, (9R,10S)- (9CI) (CA INDEX NAME)

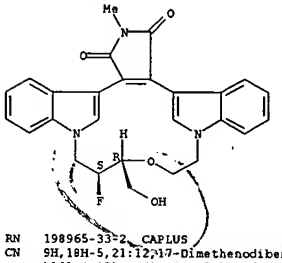
Absolute stereochemistry.



RN 198965-28-5 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-

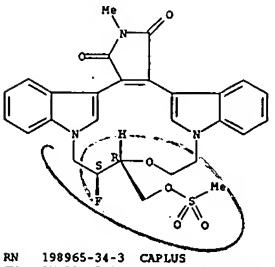
L54 ANSWER 56 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 10-fluoro-6,7,10,11-tetrahydro-9-(hydroxymethyl)-19-methyl-, (9R,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 198965-33-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 10-fluoro-6,7,10,11-tetrahydro-19-methyl-9-[[(methylsulfonyl)oxy]methyl]-, [9R-(9R*,10S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

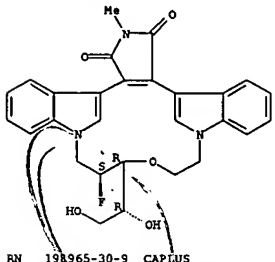


RN 198965-34-3 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-10-fluoro-6,7,10,11-tetrahydro-19-methyl-, [9R-(9R*,10S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

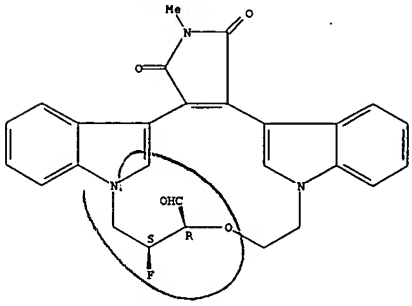
L54 ANSWER 56 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(1R)-1,2-dihydroxyethyl]-10-fluoro-6,7,10,11-tetrahydro-19-methyl-, (9R,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



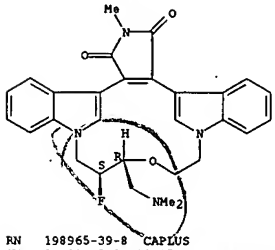
RN 198965-30-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-9-carboxaldehyde, 10-fluoro-6,7,10,11,19,20-hexahydro-19-methyl-18,20-dioxo-, [9R-(9R*,10S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



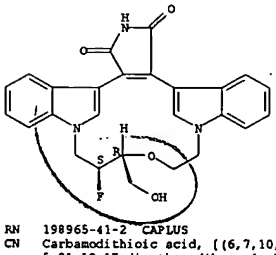
RN 198965-32-1 CAPLUS

L54 ANSWER 56 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



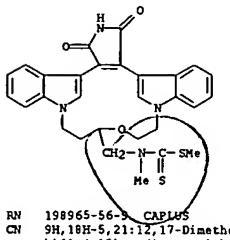
RN 198965-39-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 10-fluoro-6,7,10,11-tetrahydro-9-(hydroxymethyl)-, (9R,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



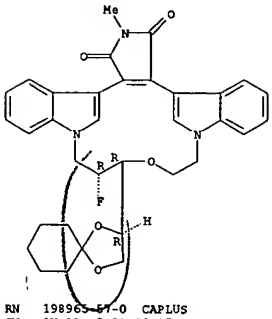
RN 198965-41-2 CAPLUS
CN Carbamodithioic acid, [(6,7,10,11,19,20-hexahydro-18,20-dioxo-9H,18H-5,21:12,17-dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecin-9-yl)methyl]methyl-, methyl ester (9CI) (CA INDEX NAME)

L54 ANSWER 56 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 198965-56-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(2R)-1,4-dioxaspiro[4.5]dec-2-yl]-10-fluoro-6,7,10,11-tetrahydro-19-methyl-, (9R,10R)- (9CI) (CA INDEX NAME)

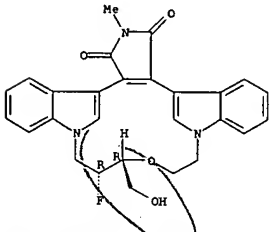
Absolute stereochemistry.



RN 198965-57-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(1R)-1,2-dihydroxyethyl]-10-fluoro-6,7,10,11-tetrahydro-19-methyl-, (9R,10R)- (9CI) (CA INDEX NAME)

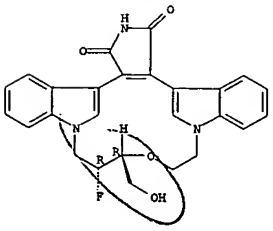
Absolute stereochemistry.

L54 ANSWER 56 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

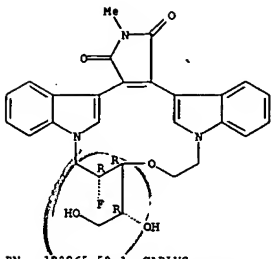


RN 198965-62-7 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 10-fluoro-6,7,10,11-tetrahydro-9-(hydroxymethyl)-, (9R,10R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

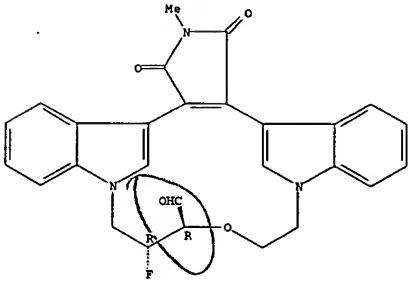


L54 ANSWER 56 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 198965-58-1 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-9-carboxaldehyde, 10-fluoro-6,7,10,11,19,20-hexahydro-19-methyl-18,20-dioxo-, [9R-(9R*,10R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



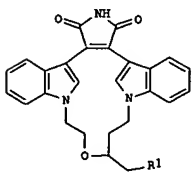
RN 198965-59-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 10-fluoro-6,7,10,11-tetrahydro-9-(hydroxymethyl)-19-methyl-, (9R,10R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 57 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:467666 CAPLUS
DOCUMENT NUMBER: 127:81470
TITLE: Preparation of intermediates for N,N'-bridged bisindolylmaleimides.
INVENTOR(S): Faul, Margaret Mary; Krumrich, Christine Ann; Winneroski, Leonard Larry, Jr.
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 776899	A1	19970604	EP 1996-308317	19961118
EP 776899	B1	20000329		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2237401	AA	19970529	CA 1996-2237401	19961118
WO 9719080	A1	19970529	WO 1996-US18518	19961118
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9677388	A1	19970611	AU 1996-77388	19961118
AU 701659	B2	19990204		
ZA 9609645	A	19980518	ZA 1996-9645	19961118
CN 1207740	A	19990210	CN 1996-199575	19961118
CN 1066734	B	20010606		
BR 9611709	A	19990223	BR 1996-11709	19961118
JP 2000500496	T2	20000118	JP 1997-519838	19961118
AT 191219	E	20000415	AT 1996-308317	19961118
ES 2145978	T3	20000716	ES 1996-308317	19961118
PL 184728	B1	20021231	PL 1996-326753	19961118
NO 9802105	A	19980508	NO 1998-2105	19980508

PRIORITY APPLN. INFO.: US 1995-7345P P 19951120
WO 1996-US18518 W 19961118
OTHER SOURCE(S): MARPAT 127:81470
GI



I

L54 ANSWER 57 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

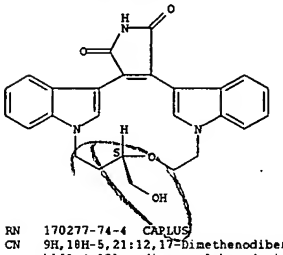
AB Title compds. (I; R1 = Br, iodo, tosyloxy), are claimed. Thus, 2,3-bis(1H-indol-3-yl)-N-methylmaleimide and (S)-3-[2-[(methylsulfonyl)oxy]ethoxy]-4-triphenylmethoxy-1-butanol methanesulfonate (prepn. given) in DMF were added over 70 h to a 50.degree. slurry of Cs2CO3 in DMF to give 57% (S)-10,11,14,15-tetrahydro-2-methyl-13-[(triphenylmethoxy)methyl]-4,9:16,21-dimetheno-1H,13H-dibenzo[E,K]pyrrolo[3,4-H][1,4,13]oxadiazacyclohexadecine-1,3(2H)-dione. The latter was converted to (S)-10,11,14,15-tetrahydro-13-(hydroxymethyl)-4,9:16,21-dimetheno-1H,13H-dibenzo[E,K]pyrrolo[3,4-H][1,4,13]oxadiazacyclohexadecine-1,3(2H)-dione, which in CH2Cl2 was treated with a soln. prepd. from Br2, pyridine, and tri-Ph phosphite in CH2Cl2 at -5.degree. to room temp. over 12-16 h to give 85-90% (S)-10,11,14,15-tetrahydro-13-(bromomethyl)-4,9:16,21-dimetheno-1H,13H-dibenzo[E,K]pyrrolo[3,4-H][1,4,13]oxadiazacyclohexadecine-1,3(2H)-dione.

IT **169940-55-0P 170277-74-4P 170277-76-6P**
191848-29-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of intermediates for N,N'-bridged bisindolylmaleimides)

RN 169940-55-0 CAPLUS

CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(hydroxymethyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

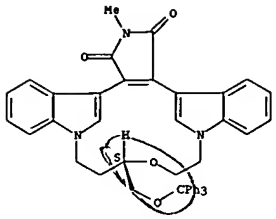


RN 170277-74-4 CAPLUS

CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-19-methyl-9-[(triphenylmethoxy)methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

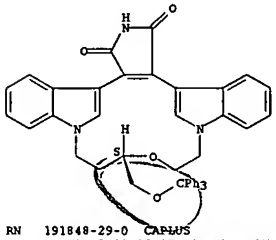
L54 ANSWER 57 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 170277-76-6 CAPLUS

CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[(triphenylmethoxy)methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

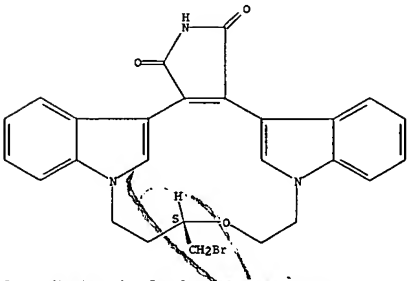


RN 191848-29-0 CAPLUS

CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-(bromomethyl)-6,7,10,11-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 57 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

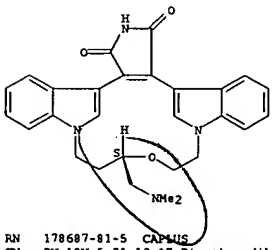


IT **169939-94-0P 178697-81-5P 191848-30-3P**
191848-31-4P 191848-32-5P 191848-33-6P
191848-39-2P 191848-41-6P 191848-44-9P
191848-45-0P 191848-48-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of intermediates for N,N'-bridged bisindolylmaleimides)

RN 169939-94-0 CAPLUS

CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

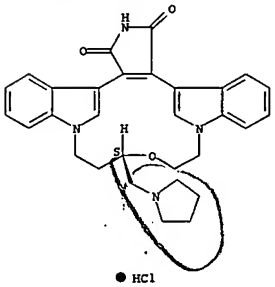


RN 178697-81-5 CAPLUS

CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(1-pyrrolidinylmethyl)-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

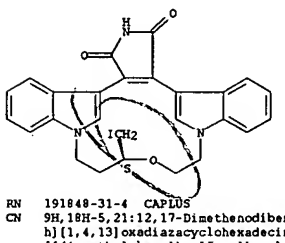
L54 ANSWER 57 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 191848-30-3 CAPLUS

CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(iodomethyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

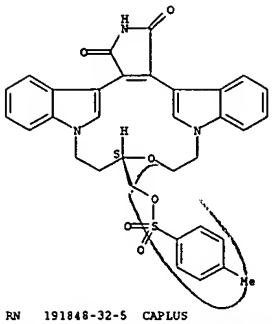


RN 191848-31-4 CAPLUS

CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[(4-methylphenyl)sulfonyl]oxy]-, (S)- (9CI) (CA INDEX NAME)

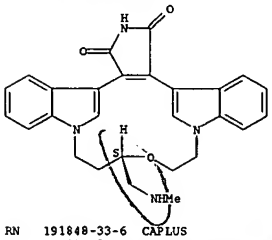
Absolute stereochemistry.

L54 ANSWER 57 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 191848-32-5 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[(methylamino)methyl]-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

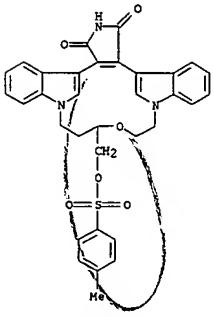


RN 191848-33-6 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[(phenylmethyl)amino]methyl]-, (S)- (9CI) (CA INDEX NAME)

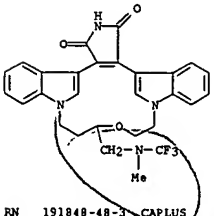
Absolute stereochemistry.

L54 ANSWER 57 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

RN 191848-44-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[[(4-methylphenyl)sulfonyl]oxy]methyl]- (9CI) (CA INDEX NAME)

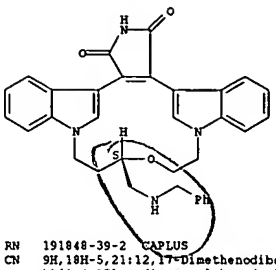


RN 191848-45-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[methyl(trifluoromethyl)amino]methyl]- (9CI) (CA INDEX NAME)

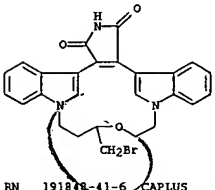


RN 191848-48-3 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[(trifluoromethyl)amino]methyl]- (9CI) (CA INDEX NAME)

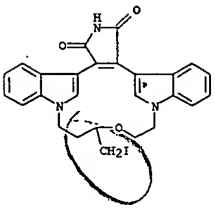
L54 ANSWER 57 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



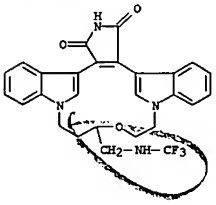
RN 191848-39-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-(bromomethyl)-6,7,10,11-tetrahydro- (9CI) (CA INDEX NAME)



RN 191848-41-6 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(iodomethyl)- (9CI) (CA INDEX NAME)



L54 ANSWER 57 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



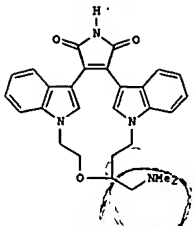
L54 ANSWER 58 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:457045 CAPLUS
DOCUMENT NUMBER: 127:95299
TITLE: Preparation of dimethenodibenzopyrrolooxadiazacyclohexadecinediones as protein kinase C inhibitors
INVENTOR(S): Engel, Gary Lowell; Farid, Nagy Alphonse; Faul, Margaret Mary; Jirousek, Michael Robert; Richardson, Lori Ann; Winneroski, Leonard Larry, Jr.
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 776895	A1	19970604	EP 1996-308318	19961118
EP 776895	B1	19981014		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2237221	AA	19970529	CA 1996-2237221	19961118
CA 2237221	C	20030325		
WO 9718809	A1	19970529	WO 1996-US18512	19961118
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9710548	A1	19970611	AU 1997-10548	19961118
AU 711125	B2	19991007		
ZA 9609646	A	19980518	ZA 1996-9646	19961118
AT 172199	E	19981015	AT 1996-308318	19961118
ES 2122764	T3	19981216	ES 1996-308318	19961118
CN 1202825	A	19981223	CN 1996-198420	19961118
CN 1093759	B	20021106		
JP 11500149	T2	19990106	JP 1996-519836	19961118
BR 9611724	A	19990601	BR 1996-11724	19961118
TW 403754	B	20000901	TW 1996-85114103	19961118
JP 3348859	B2	20021120	JP 1997-519836	19961118
PL 184715	B1	20021231	PL 1996-326754	19961118
NO 9802182	A	19980513	NO 1998-2182	19980513

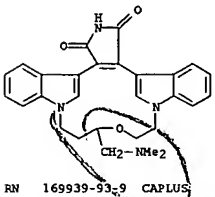
PRIORITY APPLN. INFO.: US 1995-6970P P 19951120
WO 1996-US18512 W 19961118

GI

L54 ANSWER 58 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



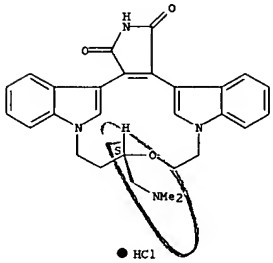
AB The methanesulfonate of title compd. (S)-I was prepd. and found to have superior soly. and bioavailability.
IT **169939-91-7P 169939-93-9P 169939-94-0P**
191937-15-2P 192050-59-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of dimethenodibenzopyrrolooxadiazacyclohexadecinediones as protein kinase C inhibitors)
RN 169939-91-7 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro- (9CI) (CA INDEX NAME)



RN 169939-93-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, (9S)-(9CI) (CA INDEX NAME)

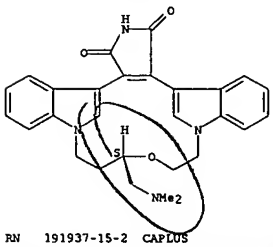
Absolute stereochemistry.

L54 ANSWER 58 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

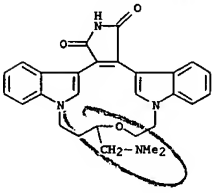


RN 191937-15-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 169939-91-7
CMF C28 H28 N4 O3

L54 ANSWER 58 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



CM 2

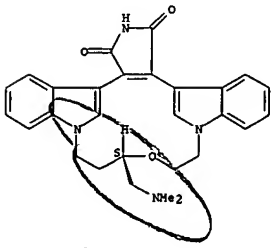
CRN 75-75-2
CMF C H4 O3 S

RN 192050-59-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (S)-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 169939-94-0
CMF C28 H28 N4 O3

Absolute stereochemistry.



CM 2

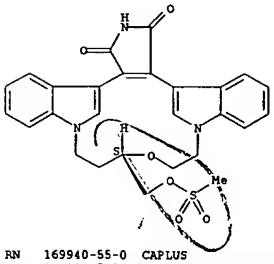
L54 ANSWER 58 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

CRN 75-75-2
CMF C H4 O3 S

IT 169940-46-8P 169940-55-0P 170277-74-4P
170277-76-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of dimethenodibenzopyrrolooxadiazacyclohexadecinediones as protein kinase C inhibitors)

RN 169940-46-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[(methylsulfonyl)oxy]methyl]-, (S)- (9CI) (CA INDEX NAME)

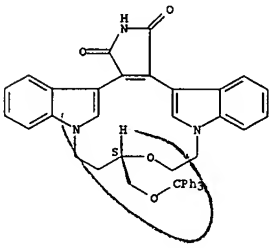
Absolute stereochemistry.



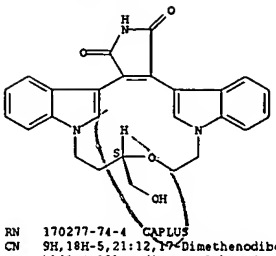
RN 169940-55-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(hydroxymethyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 58 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

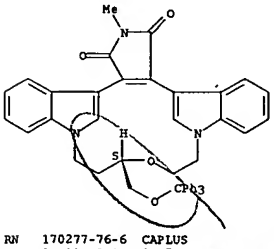


L54 ANSWER 58 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 170277-74-4 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-19-methyl-9-[(triphenylmethoxy)methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 170277-76-6 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[(triphenylmethoxy)methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 59 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:344789 CAPLUS
DOCUMENT NUMBER: 127:17847
TITLE: Staurosporine analogs as protein kinase C inhibitors
INVENTOR(S): Heath, William F., Jr.; Jirousek, Michael R.; Mcdonald, Iii John H.; Rito, Christopher J.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: U.S., 44 pp., Cont.-in-part of U.S. Ser. No. 316,973, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

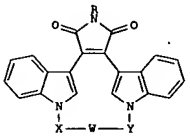
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5624949	A	19970429	US 1995-413735	19950330
CA 2137203	AA	19950608	CA 1994-2137203	19941202
FI 9405706	A	19950608	FI 1994-5706	19941202
NO 9404643	A	19950608	NO 1994-4643	19941202
AU 9479188	A1	19950615	AU 1994-79188	19941202
AU 687909	B2	19980305		
BR 9404831	A	19950808	BR 1994-4831	19941202
JP 07215977	A2	19950815	JP 1994-299399	19941202
CN 1111247	A	19951108	CN 1994-119362	19941202
CN 1050844	B	20000329		
HU 71130	A2	19951128	HU 1994-3468	19941202
HU 219709	B	20010628		
RU 2147304	C1	20000410	RU 1994-42922	19941202
TW 425397	B	20010311	TW 1994-83111226	19941202
AT 204579	E	20010915	AT 1994-308947	19941202
PL 182124	B1	20011130	PL 1994-306084	19941202
ES 2162843	T3	20020116	ES 1994-308947	19941202
CZ 291950	B6	20030618	CZ 1994-3018	19941202
BR 9502611	A	19961001	BR 1995-2611	19950531
US 5552396	A	19960903	US 1995-457000	19950601
US 5621098	A	19970415	US 1995-457657	19950601
US 5674862	A	19971007	US 1995-457060	19950601
EP 735038	A1	19961002	EP 1996-302142	19960328
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2216535	AA	19961003	CA 1996-2216535	19960328
CA 2216535	C	20020507		
WO 9630048	A1	19961003	WO 1996-US4245	19960328
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9653249	A1	19961016	AU 1996-53249	19960328
AU 701988	B2	19990211		
CN 1185742	A	19980624	CN 1996-194257	19960328
CN 1093767	B	20021106		
JP 11507327	T2	19990629	JP 1996-529640	19960328
CZ 286301	B6	20000315	CZ 1997-3051	19960328
PL 183600	B1	20020628	PL 1996-322584	19960328
US 5696108	A	19971209	US 1996-646703	19960506
US 5719175	A	19980217	US 1996-646708	19960506
US 5780461	A	19980714	US 1996-643710	19960506

L54 ANSWER 59 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

US 5723456	A	19980303	US 1996-662623		19960613
US 5698578	A	19971216	US 1996-734292		19961021
US 5739322	A	19980414	US 1997-822255		19970320
US 5843935	A	19981201	US 1997-903236		19970712
NO 9704453	A	19971119	NO 1997-4453		19970926
US 5821365	A	19981013	US 1997-971115		19971114
US 6057440	A	20000502	US 1997-970891		19971114
CN 1220266	A	19990623	CN 1997-126094		19971209
CN 1055089	B	20000802			
HK 1013827	A1	20020705	HK 1998-115199		19981223
FI 2000000516	A	20000307	FI 2000-516		20000307
FI 2001001109	A	20010528	FI 2001-1109		20010528
PRIORITY APPLN. INFO.:			US 1993-163060	B2	19931207
			US 1994-316973	B2	19941003
			US 1995-413735	A3	19950330
			US 1995-457060	A1	19950601
			US 1995-457657	A3	19950601
			WO 1996-US4245	W	19960328
			US 1996-643706	A2	19960506
			US 1996-643707	B1	19960506
			US 1997-822255	A3	19970320

OTHER SOURCE(S): MARPAT 127:17847

GI



I

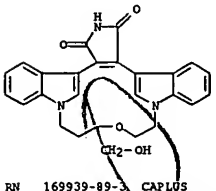
AB Staurosporine analogs I [R = H, Ac, NH2, OH; W = O, S, SO, SO2, CO, alkylene, (un)substituted NH, NOH, CONH, NHCO, arom., heterocyclic; X, Y = (un)substituted alkylene; and the benzene rings may be further substituted] were prepd. Thus, I [R = H, X = CH2CH2, W = O, Y = (S)-CH(CH2NMe2.HCl)CH2CH2, II] was prepd. from (S)-Me3CSiPh2OCH2CH(OH)CH2CO2Me, Cl3CC(:NH)OCH2CH:CH2, and the diindolylpyrroledione in 8 steps. II had IC50 for protein kinase C.alpha., C.beta.1, and C.beta.2 of 0.36, 0.0047, and 0.0059 .mu.M, resp.

IT 169939-87-1P 169939-89-3P 169939-90-6P
169939-93-9P 169940-32-3P 169940-33-4P
178687-79-1P 178687-80-4P 178687-81-5P
178687-82-6P 178687-84-8P 178687-85-9P
189635-75-4P 189635-86-7P 189635-88-9P
189635-95-8P 190265-61-3P 190266-03-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

L54 ANSWER 59 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
(prepn. of bridged diindolylpyrrolediones as protein kinase C inhibitors)

RN 169939-87-1 CAPLUS

CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(hydroxymethyl)- (9CI) (CA INDEX NAME)

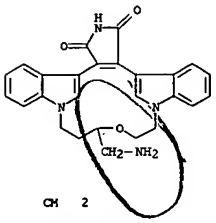


RN 169939-89-3 CAPLUS

CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-(aminomethyl)-6,7,10,11-tetrahydro-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 169939-88-2
CMF C26 H24 N4 O3



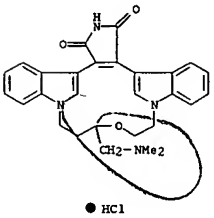
CM 2

CRN 76-05-1
CMF C2 H F3 O2

L54 ANSWER 59 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

RN 169939-90-6 CAPLUS

CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride (9CI) (CA INDEX NAME)



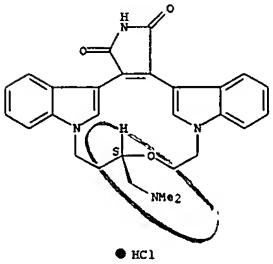
● HCl

RN 169939-93-9 CAPLUS

CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 59 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

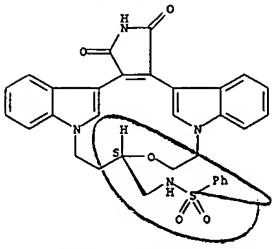


● HCl

RN 169940-32-3 CAPLUS

CN Benzenesulfonamide, N-[(6,7,10,11,19,20-hexahydro-18,20-dioxo-9H,18H-5,21:12,17-dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecin-9-yl)methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

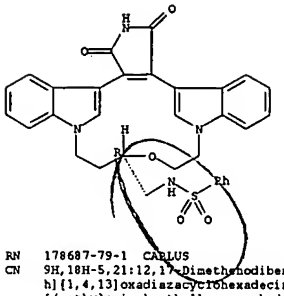


RN 169940-33-4 CAPLUS

CN Benzenesulfonamide, N-[(6,7,10,11,19,20-hexahydro-18,20-dioxo-9H,18H-5,21:12,17-dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecin-9-yl)methyl]-, (R)- (9CI) (CA INDEX NAME)

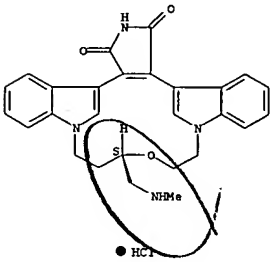
Absolute stereochemistry.

L54 ANSWER 59 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 178687-79-1 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[(methylamino)methyl]-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

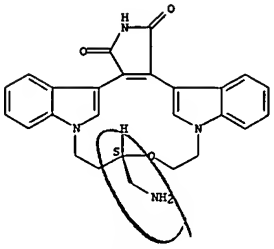


● HCl

RN 178687-80-4 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-(aminomethyl)-6,7,10,11-tetrahydro-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

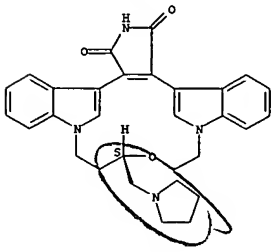
L54 ANSWER 59 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



● HCl

RN 178687-81-5 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(1-pyrrolidinylmethyl)-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

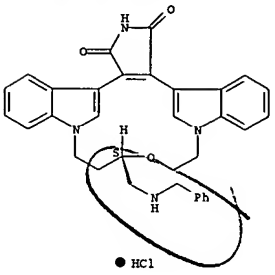


● HCl

RN 178687-82-6 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[(phenylmethyl)amino]methyl]-, monohydrochloride, (S)- (9CI) (CA INDEX

L54 ANSWER 59 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
NAME)

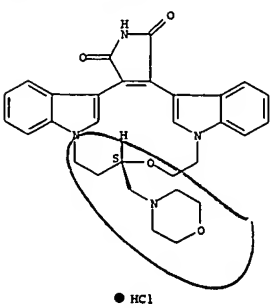
Absolute stereochemistry.



● HCl

RN 178687-84-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(4-morpholinylmethyl)-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

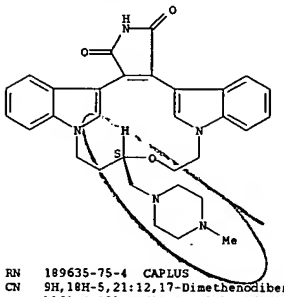


● HCl

RN 178687-85-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[(4-methyl-1-piperazinyl)methyl]-, monohydrochloride, (S)- (9CI) (CA

L54 ANSWER 59 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
INDEX NAME)

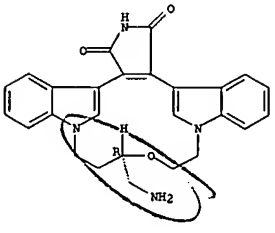
Absolute stereochemistry.



● HCl

RN 189635-75-4 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-(aminomethyl)-6,7,10,11-tetrahydro-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

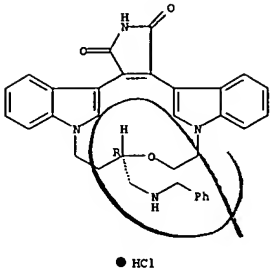


● HCl

RN 189635-86-7 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[(phenylmethyl)amino]methyl]-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

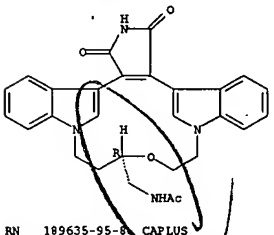
L54 ANSWER 59 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



● HCl

RN 189635-88-9 CAPLUS
CN Acetamide, N-[(6,7,10,11,19,20-hexahydro-18,20-dioxo-9H,18H-5,21:12,17-dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecin-9-yl)methyl]-, (R)- (9CI) (CA INDEX NAME)

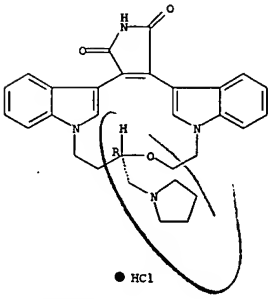
Absolute stereochemistry.



RN 189635-95-8 CAPLUS
CN Carbamic acid, [(6,7,10,11,19,20-hexahydro-18,20-dioxo-9H,18H-5,21:12,17-dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecin-9-yl)methyl]-, phenylmethyl ester, (R)- (9CI) (CA INDEX NAME)

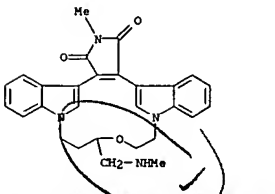
Absolute stereochemistry.

L54 ANSWER 59 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



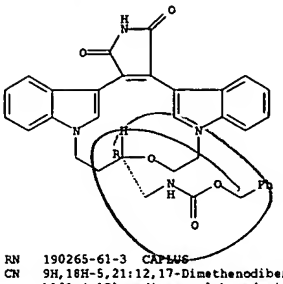
● HCl

IT 189636-12-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of bridged diindolylpyrrolediones as protein kinase C inhibitors)
RN 189636-12-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-19-methyl-9-[(methylamino)methyl]- (9CI) (CA INDEX NAME)



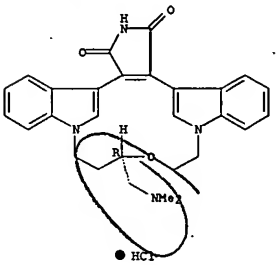
IT 169939-92-8P 169939-94-0P 169940-46-9P
169940-49-2P 169940-55-0P 169940-80-1P
169940-85-6P 189635-80-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of bridged diindolylpyrrolediones as protein kinase C inhibitors)
RN 169939-92-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

L54 ANSWER 59 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 190265-61-3 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, (9R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

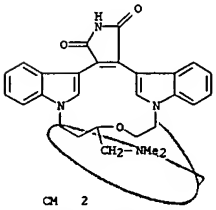
RN 190266-03-6 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(1-pyrrolidinylmethyl)-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 59 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

CM 1

CRN 169939-91-7
CMF C28 H28 N4 O3

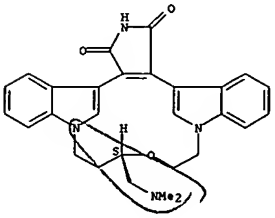


CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

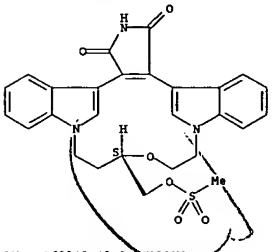
Absolute stereochemistry.



RN 169940-46-9 CAPLUS

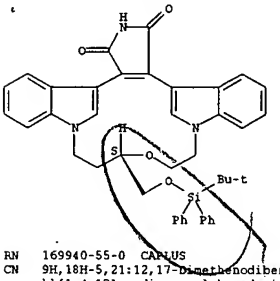
L54 ANSWER 59 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[(methylsulfonyl)oxy]methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



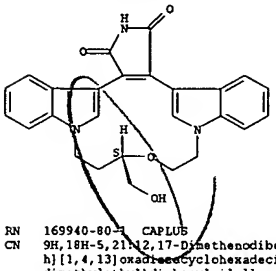
RN 169940-49-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-6,7,10,11-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

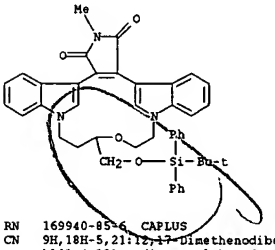


RN 169940-55-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(hydroxymethyl)-, (S)- (9CI) (CA INDEX NAME)

L54 ANSWER 59 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
Absolute stereochemistry.

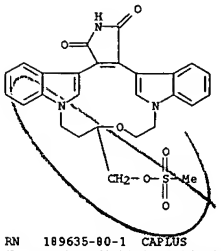


RN 169940-80-7 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-6,7,10,11-tetrahydro-19-methyl- (9CI) (CA INDEX NAME)

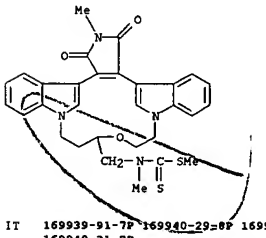


RN 169940-85-6 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[(methylsulfonyl)oxy]methyl]- (9CI) (CA INDEX NAME)

L54 ANSWER 59 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

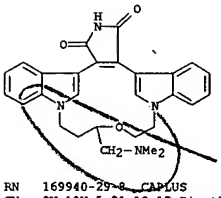


RN 189635-80-1 CAPLUS
CN Carbamodithioic acid, [(6,7,10,11,19,20-hexahydro-19-methyl-18,20-dioxo-9H,18H-5,21:12,17-dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecin-9-yl)methyl]methyl-, methyl ester (9CI) (CA INDEX NAME)



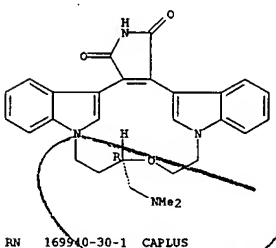
IT 169939-91-7P 169940-29-8P 169940-30-1P
169940-31-2P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of bridged diindolylpyrroledione as protein kinase C inhibitors)
RN 169939-91-7 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro- (9CI) (CA INDEX NAME)

L54 ANSWER 59 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 169940-29-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9R)- (9CI) (CA INDEX NAME)

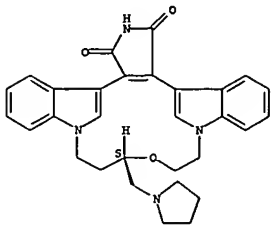
Absolute stereochemistry.



RN 169940-30-1 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(1-pyrrolidinylmethyl)-, (S)- (9CI) (CA INDEX NAME)

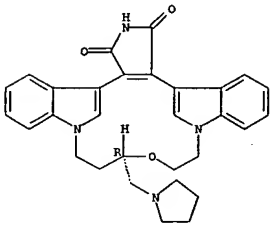
Absolute stereochemistry.

L54 ANSWER 59 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



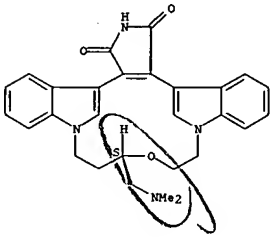
RN 169940-31-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(1-pyrrolidinylmethyl)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L54 ANSWER 60 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:175486 CAPLUS
DOCUMENT NUMBER: 126:258239
TITLE: Mechanisms of glucose toxicity. New hope for prevention of diabetic complications?
AUTHOR(S): Dutour, Anne
CORPORATE SOURCE: Laboratoire de Neuroendocrinologie, INSERM U 297, Marseille, Fr.
SOURCE: European Journal of Endocrinology (1997), 136(1), 39-40
CODEN: EJOEEP; ISSN: 0804-4643
PUBLISHER: BioScientifica
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 3 refs.
IT 169939-94-0, LY333531
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanisms of glucose toxicity in relation to prevention of diabetic complications)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

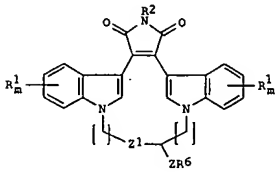
Absolute stereochemistry.



L54 ANSWER 61 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:685338 CAPLUS
DOCUMENT NUMBER: 125:328740
TITLE: Preparation of bis(indolo)macrocycles as protein kinase C inhibitors
INVENTOR(S): Heath, William Francis, Jr.; Jirousek, Michael Robert; McDonald, John Hampton; Rito, Christopher John
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 735038	A1	19961002	EP 1996-302142	19960328
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5624949	A	19970429	US 1995-413735	19950330
PRIORITY APPLN. INFO.:			US 1995-413735	A 19950330
			US 1993-163060	B2 19931207
			US 1994-316973	B2 19941003
OTHER SOURCE(S):		MARPAT 125:328740		

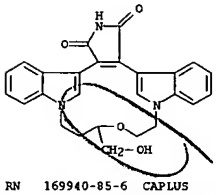
GI



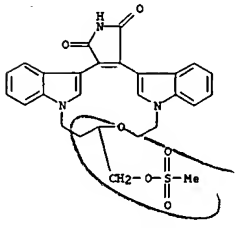
I

AB Title compds. [I; R1 = H, halo, alkyl, alkoxy, etc.; R2 = H, OH, NH2, Ac; R6 = NHCF3, NMeCF3; Z = (CH2)p, (CH2)pO(CH2)p; Z1 = O, S, NH; m = 0-3; p = 0-2] were prepd. I had IC50 of <100.mu.M against protein kinase C.
IT 169939-87-1P 169940-85-6P 180637-81-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of bis(indolo)macrocycles as protein kinase C inhibitors)
RN 169939-87-1 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(hydroxymethyl)- (9CI) (CA INDEX NAME)

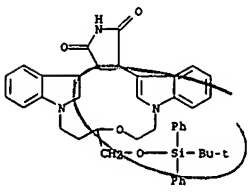
L54 ANSWER 61 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 169940-85-6 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[(methylsulfonyl)oxy]methyl]- (9CI) (CA INDEX NAME)



RN 180637-81-4 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-6,7,10,11-tetrahydro- (9CI) (CA INDEX NAME)

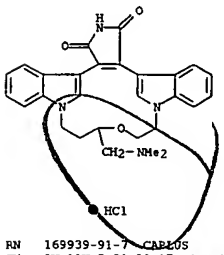


L54 ANSWER 61 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

IT **169939-90-6P 169939-91-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of bis(indolo)macrocycles as protein kinase C inhibitors)

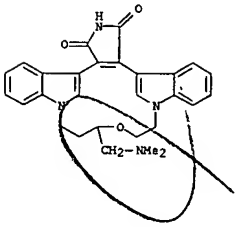
RN 169939-90-6 CAPLUS

CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride (9CI) (CA INDEX NAME)



RN 169939-91-7 CAPLUS

CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro- (9CI) (CA INDEX NAME)



L54 ANSWER 62 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN

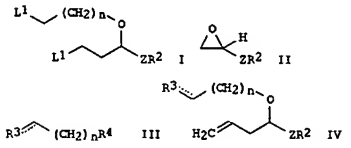
ACCESSION NUMBER: 1996:524266 CAPLUS
DOCUMENT NUMBER: 125:194997
TITLE: Synthesis of intermediates for bisindolylmaleimides
INVENTOR(S): Faul, Margaret M.; Jirousek, Michael R.; Winneroski, Leonard L., II
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 12 pp., Cont.-in-part of U.S. Ser. No. 163,060, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5541347	A	19960730	US 1994-317140	19941003
CA 2137205	AA	19950608	CA 1994-2137205	19941202
EP 657411	A1	19950614	EP 1994-308948	19941202
EP 657411	B1	19990609		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
BR 9404830	A	19950808	BR 1994-4830	19941202
HU 69164	A2	19950828	HU 1994-3467	19941202
JP 07238044	A2	19950912	JP 1994-299401	19941202
FI 9405705	A	19960603	FI 1994-5705	19941202
ZA 9409611	A	19960603	ZA 1994-9611	19941202
IL 111851	A1	19980924	IL 1994-111851	19941202
AT 181049	E	19990615	AT 1994-308948	19941202
ES 2134910	T3	19991016	ES 1994-308948	19941202
US 5614647	A	19970325	US 1995-452613	19950525
US 5665877	A	19970909	US 1996-650922	19960517
US 5698578	A	19971216	US 1996-734292	19961021

PRIORITY APPLN. INFO.: US 1993-163060 B2 19931207
US 1994-316973 B2 19941003
US 1994-317140 A 19941003
US 1995-452613 A3 19950525
US 1995-457060 A1 19950601

OTHER SOURCE(S): MARPAT 125:194997

GI



L54 ANSWER 62 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

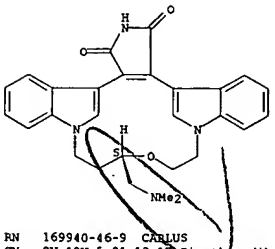
AB The title compds. [I; L1 = leaving group; R2 = N3, protected NH or OH; Z = (CH2)n; n = 1-3] are prepd. by the alkylation of and epoxide II with a Li acetylide, a Ce acetylide, vinyl cuprate, vinyl aluminum, vinyl tin, vinyl lithium, or a vinyl Grignard to produce alkene H2C:CHCH2CH(OH)ZR2 which is reacted with a compd. (III; R3 = halogen, protected OH; R4 = Cl, Br, I) to form intermediate IV which is converted into I.

IT **169939-94-0P 169940-46-9P 169940-55-0P**
170277-74-4P 170277-76-6P 180637-81-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of intermediates for bisindolylmaleimides)

RN 169939-94-0 CAPLUS

CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

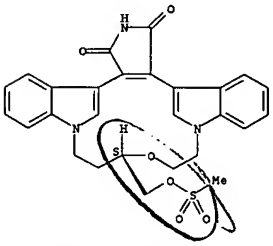


RN 169940-46-9 CAPLUS

CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[(methylsulfonyl)oxy]methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

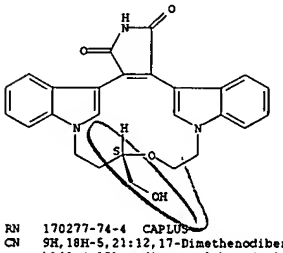
L54 ANSWER 62 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 169940-55-0 CAPLUS

CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(hydroxymethyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

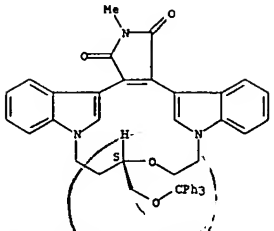


RN 170277-74-4 CAPLUS

CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-19-methyl-9-[(triphenylmethoxy)methyl]-, (S)- (9CI) (CA INDEX NAME)

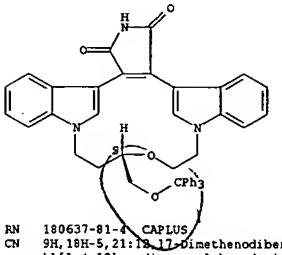
Absolute stereochemistry.

L54 ANSWER 62 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



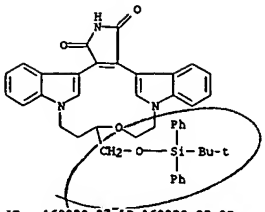
RN 170217-76-6 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[(triphenylmethoxy)methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

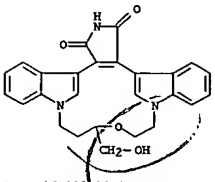


RN 180637-81-4 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-6,7,10,11-tetrahydro- (9CI) (CA INDEX NAME)

L54 ANSWER 62 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



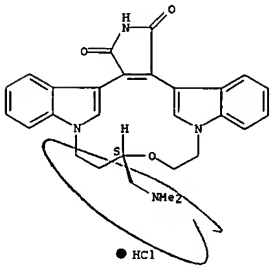
IT 169939-87-1P 169939-93-9P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of intermediates for bisindolylmaleimides)
RN 169939-87-1 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(hydroxymethyl)- (9CI) (CA INDEX NAME)



RN 169939-93-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 62 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



L54 ANSWER 63 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN

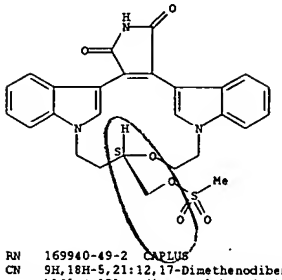
ACCESSION NUMBER: 1996:354134 CAPLUS
DOCUMENT NUMBER: 125:75324
TITLE: (S)-13-[(Dimethylamino)methyl]-10,11,14,15-tetrahydro-4,9:16,21-dimetheno-1H,13H-dibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecene-1,3(2H)-dione (LY333531) and Related Analogs: Isoenzyme Selective Inhibitors of Protein Kinase C.beta.
AUTHOR(S): Jirousek, Michael R.; Gillig, James R.; Gonzalez, Cecile M.; Heath, William F.; McDonald, John H., III; Neel, David A.; Rito, Christopher J.; Singh, Upinder; Stramm, Lawrence E.; et al.
CORPORATE SOURCE: Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, 46285, USA
SOURCE: Journal of Medicinal Chemistry (1996), 39(14), 2664-2671
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 125:75324

AB Protein kinase C (PKC) is a family of closely related serine and threonine kinases. Overactivation of some PKC isoenzymes has been postulated to occur in several disease states, including diabetic complications. Selective inhibition of overactivated PKC isoenzymes may offer a unique therapeutic approach to disease states such as diabetic retinopathy. A novel series of 14-membered macrocycles contg. a N-N'-bridged bisindolylmaleimide moiety is described. A panel of eight cloned human PKC isoenzymes (.alpha., .beta.I, .beta.II, .gamma., .delta., .epsilon., .zeta., .eta.) was used to identify the series and optimize the structure and assocd. activity relation. The dimethylamine analog LY333531, (S)-13-[(dimethylamino)methyl]-10,11,14,15-tetrahydro-4,9:16,21-dimetheno-1H,13H-dibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecene-1,3(2H)-dione, inhibits the PKC.beta.I (IC50 = 4.7 nM) and PKC.beta.II (IC50 = 5.9 nM) isoenzymes and was 76- and 61-fold selective for inhibition of PKC.beta.I and PKC.beta.II in comparison to PKC.alpha., resp. The addnl. analogs described in the series are also selective inhibitors of PKC.beta.. LY333531 exhibits ATP dependent competitive inhibition of PKC.beta.I and is selective for PKC in comparison to other ATP dependent kinases (protein kinase A, calcium calmodulin, casein kinase, src tyrosine kinase). The cellular activity of the series was assessed using bovine retinal capillary endothelial cells. Retinal endothelial cell dysfunction has been implicated in the development of diabetic retinopathy. Plasminogen activator activity stimulated by a phorbol ester (4.beta.-phorbol 12,13-dibutyrate) in endothelial cells was inhibited by the compds. in the series with ED50 values ranging from 7.5 to 0.21 .mu.M. A comparison of the PKC isoenzyme and related ATP dependent kinase inhibition profiles is provided for the series and compared to the profile for staurosporine, a nonselective PKC inhibitor. The cellular activity of the series is compared with that of the kinase inhibitor staurosporine.

IT 169940-46-9P 169940-49-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of macrocyclic bisindolylmaleimide (LY333531) and related analogs as isoenzyme selective inhibitors of protein kinase C.beta. in relation to structure and diabetic retinopathy treatment)
RN 169940-46-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[(methylsulfonyl)oxy]methyl]-, (S)- (9CI) (CA INDEX NAME)

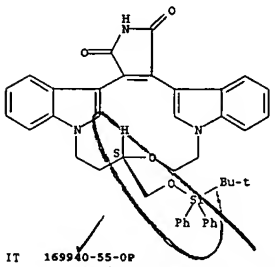
L54 ANSWER 63 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

Absolute stereochemistry.



RN 169940-49-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-6,7,10,11-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

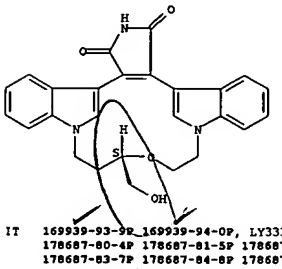


IT 169940-55-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of macrocyclic bisindolylmaleimide (LY333531) and related analogs as isoenzyme selective inhibitors of protein kinase C.beta. in relation to structure and diabetic retinopathy treatment)

L54 ANSWER 63 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

RN 169940-55-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(hydroxymethyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

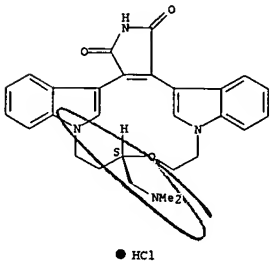


IT 169939-93-9P 169939-94-0P, LY333531 178687-79-1P
178687-80-4P 178687-81-5P 178687-82-6P
178687-83-7P 178687-84-8P 178687-85-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of macrocyclic bisindolylmaleimide (LY333531) and related analogs as isoenzyme selective inhibitors of protein kinase C.beta. in relation to structure and diabetic retinopathy treatment)

RN 169939-93-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

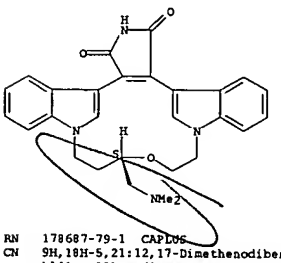
L54 ANSWER 63 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



● HCl

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

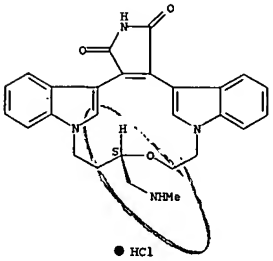
Absolute stereochemistry.



RN 178687-79-1 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[(methylamino)methyl]-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

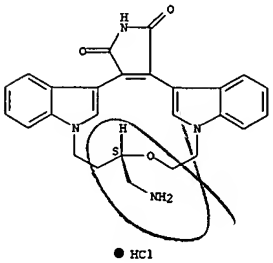
L54 ANSWER 63 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



● HCl

RN 178687-80-4 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-(aminomethyl)-6,7,10,11-tetrahydro-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

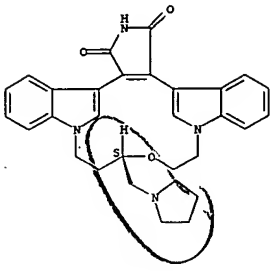


● HCl

RN 178687-81-5 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(1-pyrrolidinylmethyl)-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

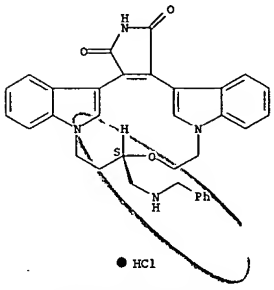
L54 ANSWER 63 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



● HCl

RN 178687-82-6 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[(phenylmethyl)amino]methyl]-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



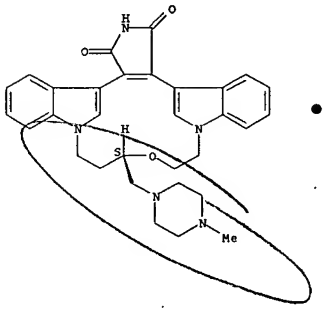
● HCl

RN 178687-83-7 CAPLUS
CN Benzenesulfonamide, N-[(6,7,10,11,19,20-hexahydro-18,20-dioxo-9H,18H-5,21:12,17-dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadec

L54 ANSWER 63 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

RN 178687-85-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[(4-methyl-1-piperazinyl)methyl]-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

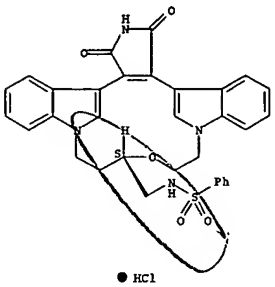
Absolute stereochemistry.



● HCl

L54 ANSWER 63 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
in-9-yl)methyl]-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

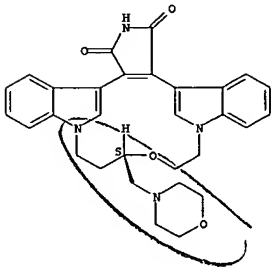
Absolute stereochemistry.



● HCl

RN 178687-84-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(4-morpholinylmethyl)-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

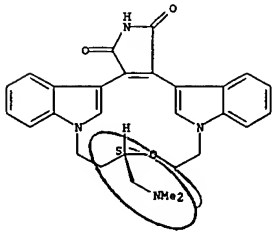
Absolute stereochemistry.



● HCl

L54 ANSWER 64 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:272548 CAPLUS
DOCUMENT NUMBER: 124:332511
TITLE: Amelioration of vascular dysfunctions in diabetic rats by an oral PKC .beta. inhibitor
AUTHOR(S): Ishii, Hidehiro; Jirousek, Michael R.; Koya, Daisuke; Takagi, Chikako; Xia, Pu; Clermont, Allen; Bursell, Sven-Erik; Kern, Timothy S.; Ballas, Lawrence M.; et al.
CORPORATE SOURCE: Dep. Med., Joslin Diabetes Cent., Boston, MA, 02215, USA
SOURCE: Science (Washington, D. C.) (1996), 272(5262), 728-31
CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The vascular complications of diabetes mellitus have been correlated with enhanced activation of protein kinase C (PKC). LY 333531, a specific inhibitor of the .beta. isoform of PKC, was synthesized and was shown to be a competitive reversible inhibitor of PKC .beta.1 and .beta.2, with a half-maximal inhibitory const. of .apprx.5 nM; this value was one-fiftieth of that for other PKC isoenzymes and one-thousandth of that for non-PKC kinases. When administered orally, LY 333531 ameliorated the glomerular filtration rate, albumin excretion rate, and retinal circulation in diabetic rats in a dose-responsive manner, in parallel with its inhibition of PKC activities.
IT **169939-94-0**, LY 333531
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amelioration of vascular dysfunctions in diabetic rats by an oral protein kinase C .beta. inhibitor)
RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L54 ANSWER 65 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:916432 CAPLUS
DOCUMENT NUMBER: 123:314034
TITLE: Improved synthesis of bisindolylmaleimides.
INVENTOR(S): Faul, Margaret Mary; Heath, William Francis, Jr.; Jirousek, Michael Robert; Mcdonald, John Hampton, III; Rito, Christopher John; Winneroski, Leonard Larry, Jr.
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 657411	A1	19950614	EP 1994-308948	19941202
EP 657411	B1	19990609		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5541347	A	19960730	US 1994-317140	19941003
US 5698578	A	19971216	US 1996-734292	19961021

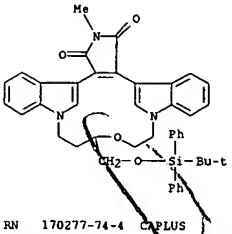
PRIORITY APPLN. INFO.: US 1993-163060 A 19931207
US 1994-317140 A 19941003
US 1994-316973 B2 19941003
US 1995-457060 A1 19950601
OTHER SOURCE(S): CASREACT 123:314034; MARPAT 123:314034
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention provides a novel synthesis of macrocyclic title compds. I [Z = (CH2)n; R = H, halo, alkyl, OH, alkoxy, haloalkyl, NO2, NR5R6, alkanoylamino; R1 = alkyl, alkoxy, OH, CO2H, cyano, SH, (un)substituted NH2, etc.; m = 0-3; n = 1-3], which are known antagonists of protein kinase C (PKC). The compds. are produced in high yield and without expensive chromatog. sepns. via the novel linking-group intermediates II [R2 = N3, protected NH2 or protected OH; L1 = leaving groups; Z = (CH2)n; n = 1-3]. The synthesis is particularly advantageous because it is stereoselective. For example, (S)-O-tritylglycidol reacted with vinylmagnesium bromide and CuI to give 96% (S)-CH2:CHCH2CH(OH)CH2OCPh3, which reacted with NaH and allyl bromide to give 98% diolefin (S)-CH2:CHCH2CH(CH2OCPh3)OCH2CH:CH2. This underwent ozonolysis and redn. with NaBH4 to give 100% diol, which was converted to 88% key intermediate (S)-II [ZR2 = CH2OCPh3, L1 = MeSO3, n = 1]. This underwent cyclization with 2,3-bis(1H-indol-3-yl)-N-methylmaleimide in DMF contg. Cs2CO3 under high-diln. conditions to give 57% cyclized product III, which was converted in 5 steps to target compd. (S)-I [R = H, m = 0, n = 1, ZR1 = CH2NMe2].

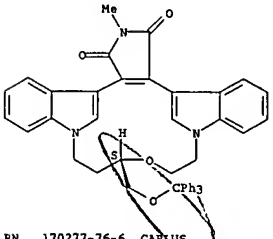
IT **169940-46-9P 169940-55-0P 169940-80-1P**
170277-74-4P 170277-76-6P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

L54 ANSWER 65 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 170277-74-4 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-19-methyl-9-[(triphenylmethoxy)methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



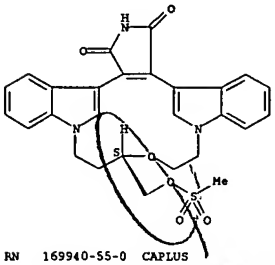
RN 170277-76-6 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[(triphenylmethoxy)methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 65 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
(intermediate; improved prepn. of bisindolylmaleimides)

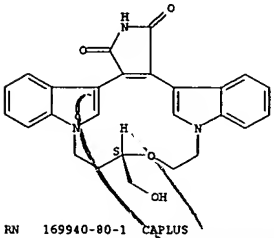
RN 169940-46-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[(methylsulfonyl)oxy]methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



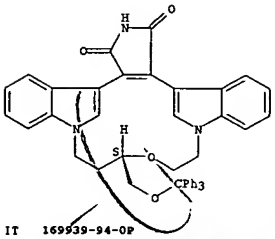
RN 169940-55-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(hydroxymethyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 169940-80-1 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-6,7,10,11-tetrahydro-19-methyl-(9CI) (CA INDEX NAME)

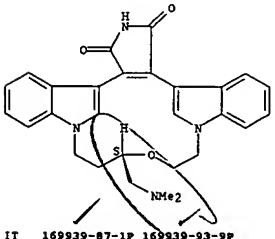
L54 ANSWER 65 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



IT **169939-94-0P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(target compd.; improved prepn. of bisindolylmaleimides)

RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

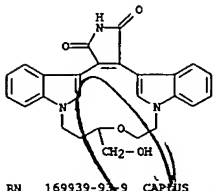
Absolute stereochemistry.



IT **169939-87-1P 169939-93-9P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(target compd.; improved prepn. of bisindolylmaleimides)

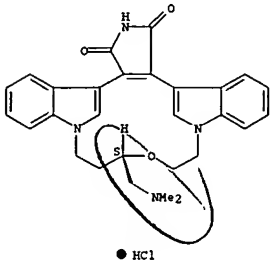
RN 169939-87-1 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(hydroxymethyl)- (9CI) (CA INDEX NAME)

L54 ANSWER 65 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 169939-93-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, (9S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

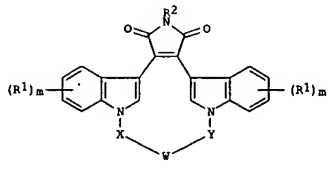
L54 ANSWER 66 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:902566 CAPLUS
DOCUMENT NUMBER: 123:314033
TITLE: Preparation of bis(indolyl)maleimide macrocycles as .beta.-isoenzyme selective protein kinase C inhibitors.
INVENTOR(S): Heath, William Francis, Jr.; Jirousek, Michael Robert; Mcdonald, John Hampton, III; Rito, Christopher John
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: Eur. Pat. Appl., 70 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 657458	A1	19950614	EP 1994-308947	19941202
EP 657458	B1	20010822		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2137203	AA	19950608	CA 1994-2137203	19941202
FI 9405706	A	19950608	FI 1994-5706	19941202
NO 9404643	A	19950608	NO 1994-4643	19941202
AU 9479188	A1	19950615	AU 1994-79188	19941202
AU 687909	B2	19980305		
BR 9404831	A	19950808	BR 1994-4831	19941202
JP 07215977	A2	19950815	JP 1994-299399	19941202
CN 1111247	A	19951108	CN 1994-119362	19941202
CN 1050844	B	20000329		
HU 71130	A2	19951128	HU 1994-3468	19941202
HU 219709	B	20010628		
RU 2147304	C1	20000410	RU 1994-42922	19941202
TW 425397	B	20010311	TW 1994-83111226	19941202
AT 204579	E	20010915	AT 1994-308947	19941202
PL 182124	B1	20011130	PL 1994-306084	19941202
ES 2162843	T3	20020116	ES 1994-308947	19941202
CZ 291950	B6	20030618	CZ 1994-3018	19941202
BR 9502611	A	19961001	BR 1995-2611	19950531
US 5698578	A	19971216	US 1996-734292	19961021
CN 1220266	A	19990623	CN 1997-126094	19971209
CN 1055089	B	20000802		
HK 1013827	A1	20020705	HK 1998-115199	19981223
FI 2000000516	A	20000307	FI 2000-516	20000307
FI 2001001109	A	20010528	FI 2001-1109	20010528

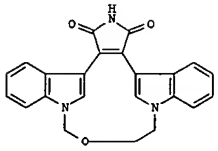
PRIORITY APPLN. INFO.: US 1993-163060 A 19931207
US 1994-316973 A 1994100 3
US 1995-457060 A1 19950601

OTHER SOURCE(S): MARPAT 123:314033
GI

L54 ANSWER 66 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



I



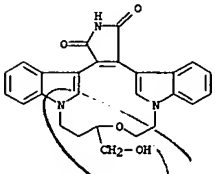
II

AB Title compds. [I; W = O, S, SO, SO2, CO, (substituted) alkylene, alkenylene, arylene, heterocyclylene, CONH, etc.; X, Y = (substituted) alkylene; XYW = (CH2)nA; A = amino acid residue; n = 2-5; R1 = H, halo, alkyl, OH, alkoxy, haloalkyl, NO2, amino, alkylcarbonylamino; R2 = H, Ac, NH2, OH; m = 0-3], were prepd. Thus, 3,4-bis(3'-indolyl)furan-2,5-dione in DMF was treated with NaH and then (BrCH2CH2)2O to give 20% cyclocondensation product, which in DMF was treated with hexamethyldisilazane in MeOH to give 72% title compd. (II). II inhibited protein kinase C .beta.-1 with IC50 = 0.05 .mu.M. I preferentially inhibit the .beta.-isoenzymes by a factor of .gtoreq.10 over other isoenzymes.

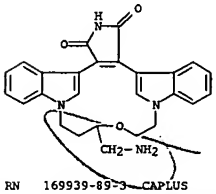
IT 169939-87-1P 169939-88-2P 169939-89-3P
169939-90-6P 169939-91-7P 169939-92-8P
169939-93-9P 169939-94-0P 169940-29-8P
169940-30-1P 169940-31-2P 169940-32-3P
169940-33-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of bis(indolyl)maleimide macrocycles as .beta.-isoenzyme selective protein kinase C inhibitors)

RN 169939-87-1 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(hydroxymethyl)- (9CI) (CA INDEX NAME)

L54 ANSWER 66 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



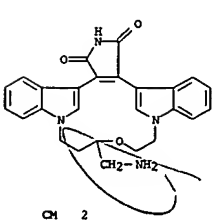
RN 169939-88-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-(aminomethyl)-6,7,10,11-tetrahydro- (9CI) (CA INDEX NAME)



RN 169939-89-3 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-(aminomethyl)-6,7,10,11-tetrahydro-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 169939-88-2
CMF C26 H24 N4 O3

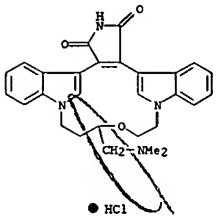


CM 2

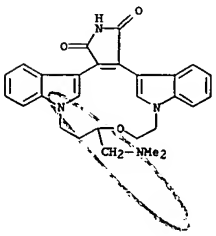
L54 ANSWER 66 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

CRN 76-05-1
CMF C2 H F3 O2

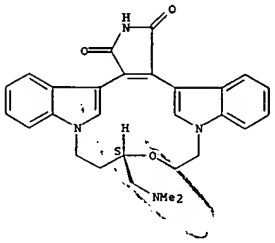
RN 169939-90-6 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride (9CI) (CA INDEX NAME)



RN 169939-91-7 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro- (9CI) (CA INDEX NAME)

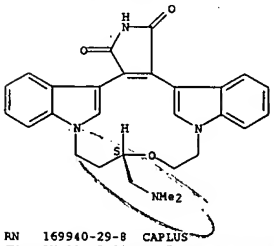


L54 ANSWER 66 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 169939-94-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



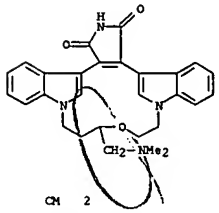
RN 169940-29-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, (9R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L54 ANSWER 66 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
RN 169939-92-8 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 169939-91-7
CMF C28 H28 N4 O3



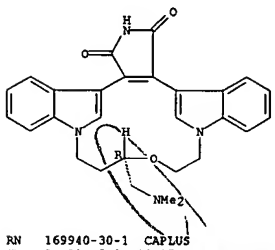
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 169939-93-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[(dimethylamino)methyl]-6,7,10,11-tetrahydro-, monohydrochloride, (9S)- (9CI) (CA INDEX NAME)

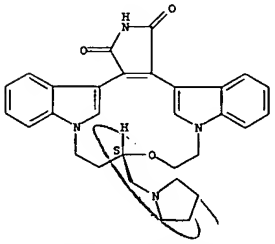
Absolute stereochemistry.

L54 ANSWER 66 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 169940-30-1 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(1-pyrrolidinylmethyl)-, (S)- (9CI) (CA INDEX NAME)

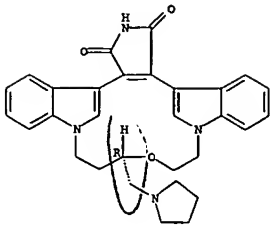
Absolute stereochemistry.



RN 169940-31-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(1-pyrrolidinylmethyl)-, (R)- (9CI) (CA INDEX NAME)

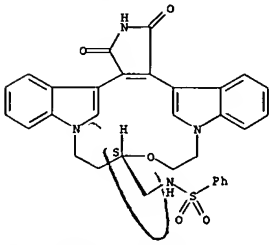
Absolute stereochemistry.

L54 ANSWER 66 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 169940-32-3 CAPLUS
CN Benzenesulfonamide, N-[(6,7,10,11,19,20-hexahydro-18,20-dioxo-9H,18H-5,21:12,17-dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecin-9-yl)methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

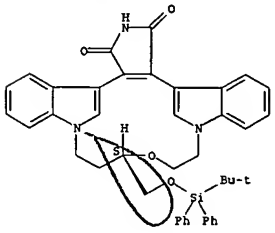


RN 169940-33-4 CAPLUS
CN Benzenesulfonamide, N-[(6,7,10,11,19,20-hexahydro-18,20-dioxo-9H,18H-5,21:12,17-dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecin-9-yl)methyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

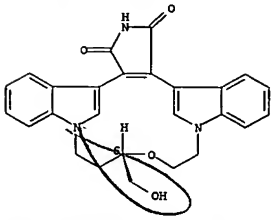
L54 ANSWER 66 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

Absolute stereochemistry.



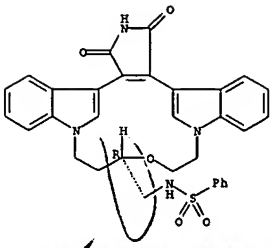
RN 169940-55-0 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(hydroxymethyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 169940-80-1 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-6,7,10,11-tetrahydro-19-methyl- (9CI) (CA INDEX NAME)

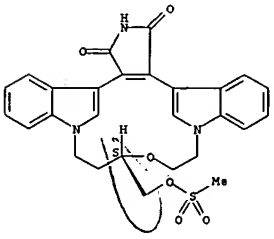
L54 ANSWER 66 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



IT 169940-46-9P 169940-49-2P 169940-55-0P
169940-80-1P 169940-85-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of bis(indolyl)maleimide macrocycles as .beta.-isoenzyme selective protein kinase C inhibitors)

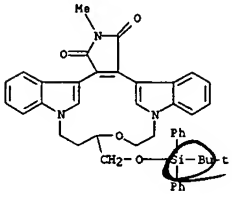
RN 169940-46-9 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[(methylsulfonyl)oxy]methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

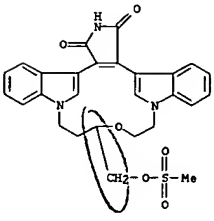


RN 169940-49-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-6,7,10,11-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

L54 ANSWER 66 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

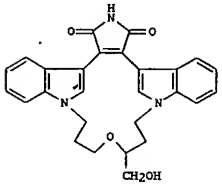


RN 169940-85-6 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-[[(methylsulfonyl)oxy]methyl]- (9CI) (CA INDEX NAME)



L54 ANSWER 67 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1995:827713 CAPLUS
DOCUMENT NUMBER: 124:29743
TITLE: Synthesis of bisindolylmaleimide macrocycles
AUTHOR(S): Jirousek, Michael R.; Gillig, James R.; Neel, David A.; Rito, Christopher J.; O'Bannon, Douglas; Heath, William F.; McDonald, John H., III; Faul, Margaret M.; Winneroski, Leonard L.
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly Co., Indianapolis, IN, 46285, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1995), 5(18), 2093-6
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 124:29743
GI



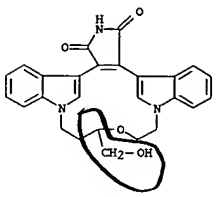
I

AB The synthesis of a novel class of N,N'-macrocyclic bisindolylmaleimides, e.g., I, is reported. The key step involves a remarkably efficient intramol. cyclization reaction. The method was further developed to provide an efficient synthesis of this type of macrocycle through an intermol. alkylation with subsequent intramol. cyclization.

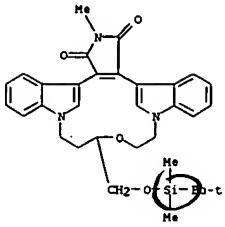
IT **171819-90-2P 171819-91-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of bisindolylmaleimide macrocycles)

RN 171819-90-2 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 9-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-6,7,10,11-tetrahydro-19-methyl- (9CI) (CA INDEX NAME)

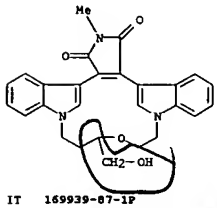
L54 ANSWER 67 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



L54 ANSWER 67 OF 67 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 171819-91-3 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(hydroxymethyl)-19-methyl- (9CI) (CA INDEX NAME)



IT **169939-87-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of bisindolylmaleimide macrocycles)

RN 169939-87-1 CAPLUS
CN 9H,18H-5,21:12,17-Dimethenodibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecine-18,20(19H)-dione, 6,7,10,11-tetrahydro-9-(hydroxymethyl)- (9CI) (CA INDEX NAME)